ভগবান ইহা বিবৃত করিলেন। ভিক্ষুগণ সন্তুষ্ট মনে ভগবানের ভাষণে আনন্দ প্রকাশ করিলেন।

অরণবিভঙ্গ সূত্র সমাপ্ত

১০. ধাতুবিভিঙ্গ সূত্র

আমি এইরূপ শুনিয়াছি।এক সময় ভগবান মগধরাজ্যে বিচরণ করিতে করিতে রাজগৃহে পৌঁছাইলেন, তারপর ভার্গব কুম্ভকারের নিকট উপস্থিত হইলেন, উপস্থিত হইয়া ভার্গব কুম্ভকারকে বলিলেন, "ভার্গব, যদি তোমার অসুবিধা না হয়, তাহা হইলে তোমার আবাসে আমি এক রাত্রি থাকিব।"

"ভদন্ত, আমার অসুবিধা নাই। একজন প্রব্রজিত প্রথম হইতে এইখানে বাসরত। যদি তিনি অনুমতি দেন, তাহা হইলে আপনি এইখানে যথেচ্ছ অবস্থান করুন।"

সেই সময়ে পুক্কুসাতি নামে এক কুলপুত্র ভগবানের প্রতি শ্রদ্ধাবশত গৃহ হইতে অনাগারিকরূপে প্রব্রজিত হইয়াছিলেন। তিনি সেই কুম্ভকারগৃহে প্রথম হইতে আসিয়া বাস করিতেছিলেন। তখন ভগবান আয়ুষ্মান পুক্কুসাতির নিকট উপস্থিত হইলেন, উপস্থিত হইয়া বলিলেন, "ভিক্ষু, যদি তোমার অসুবিধা না হয়, তাহা হইলে আমি এই আবাসে এক রাত্রি বাস করিব।"

"বন্ধু, কুম্ভকারের আবাস খুব প্রশস্ত, আয়ুষ্মান যথেচ্ছ অবস্থান করুন।" তখন ভগবান কুম্ভকারগৃহে প্রবেশ করিয়া একপার্শ্বে তৃণাসন বিছাইয়া পর্যঙ্কাবদ্ধ হইয়া দেহাগ্রভাগ ঋজুভাবে রাখিয়া পরিমুখে (লক্ষ্যাভিমুখে) স্মৃতি উপস্থাপিত করিয়া উপবেশন করিলেন। ভগবান রাত্রির বহুক্ষণ পর্যন্ত কাটাইলেন। তখন ভগবানের এইরূপ মনে হইল : "এই কুলপুত্র কি প্রসন্নভাবে আছেন? তাঁহাকে জিজ্ঞাসা করিলে কেমন হয়?" তখন ভগবান আয়ুষ্মান পুক্কুসাতিকে বলিলেন, "ভিক্ষু, কাহাকে উদ্দেশ্য করিয়া তুমি প্রব্রজিত হইয়াছ? কে তোমার শাস্তা? কাহার ধর্ম তুমি সমর্থন করো?"

বন্ধু , শ্রমণ গৌতম শাক্যপুত্র শাক্য কুল হইতে প্রব্রজিত হইয়াছেন, সেই মাননীয় গৌতমের এই প্রকার কল্যাণজনক কীর্তিশব্দ বিস্তার লাভ করিয়াছে : সেই ভগবান অর্হৎ, সম্যকসম্বুদ্ধ, বিদ্যাচরণসম্পন্ন, সুগত, লোকবিদূ, অনুত্তর পুরুষদম্যসারথি, দেব-মানবের শাস্তা, বুদ্ধ ও ভগবান; সেই ভগবানের উদ্দেশ্যেই আমি প্রব্রজিত হইয়াছি, তিনিই আমার শাস্তা ভগবানের ধর্ম আমি সমর্থন করি।

ভিক্ষু, সেই ভগবান অর্হৎ সম্যকসম্বুদ্ধ এখন কোথায় অবস্থান

করিতেছেন?

বন্ধু, উত্তর জনপদে শ্রাবস্তী নামে একটি নগর আছে, তথায়... অবস্থান করিতেছিলেন।

ভিক্ষু, সেই ভগবানকে পূর্বে কি তুমি দেখিয়াছ? দেখিয়া জানিতে পারিয়াছ কি?

না, বন্ধু, সেই ভগবানকে আমি পূর্বে দেখি নাই এবং দেখিয়া জানিতে পারি নাই।

তখন ভগবান চিন্তা করিলেন, এই কুলপুত্র আমাকে উদ্দেশ্য করিয়া প্রব্রজিত হইয়াছে, আমি ইহাকে ধর্মদেশনা করিলে কেমন হয়, তখন ভগবান আয়ুষ্মান পুক্কুসাতিকে আহ্বান করিলেন, ভিক্ষু, তোমার নিকট আমি ধর্মদেশনা করিব। উত্তমরূপে মনোনিবেশ করিয়া শ্রবণ করো, আমি বলিতেছি। "হ্যাঁ বন্ধু!" বলিয়া আয়ুষ্মান পুক্কুসাতি ভগবানকে প্রত্যুত্তর দিলেন।

ভগবান বলিলেন, ভিক্ষু, এই ব্যক্তির আছে ছয় ধাতু, ছয় স্পর্শ-আয়তন, অষ্টাদশ মন-উপবিচার, চারি অধিষ্ঠান, যেখানে স্থিতি[১] আছে মান এবং আনন্দ প্রবর্তিত হয় না, প্রবর্তিত হয় না বলিয়া মুনি শান্ত বলিয়া কথিত হয়, তাহার প্রজ্ঞার জন্য প্রমত্ত থাকা উচিত নহে, সত্য রক্ষা করা উচিত, ত্যাগ অনুশীলন করা উচিত, শান্তির জন্য শিক্ষালাভ করা উচিত। ইহাই ছয় ধাতু বিভঙ্গের উদ্দেশ।

'এই ব্যক্তির ছয় ধাতু আছে' ইহা কথিত হইয়াছে। কী কারণে ইহা কথিত হইয়াছে? পৃথিবীধাতু, আপধাতু, তেজধাতু, বায়ুধাতু, আকাশ ধাতু ও বিজ্ঞান ধাতু; এই ছয় ধাতু সম্পর্কে ইহা কথিত হইয়াছে।

'এই ব্যক্তির ছয় স্পর্শ আয়তন আছে' ইহা কথিত হইয়াছে। কী সম্পর্কে ইহা কথিত হইয়াছে? চক্ষু-সংস্পর্শ-আয়তন, শ্রোত্র-সংস্পর্শ-আয়তন, ঘ্রাণ-সংস্পর্শ-আয়তন, জিহ্বা-সংস্পর্শ-আয়তন, কায়-সংস্পর্শ-আয়তন, মন-সংস্পর্শ-আয়তন।... কথিত হইয়াছে।

'এই ব্যক্তির অষ্টাদশ মনোপবিচার আছে' ইহা কথিত হইয়াছে। কী সম্পর্কে ইহা কথিত হইয়াছে? চক্ষু দ্বারা রূপ দর্শন করিয়া সৌমনস্য স্থানীয় রূপকে উপবিচার করে (অর্থাৎ রূপ যে সৌমনস্য উৎপন্ন করে তাহা অনুভব করে), দৌর্মনস্য স্থানীয় রূপকে উপবিচার করে, উপেক্ষা স্থানীয় রূপকে

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[১]। অধিষ্ঠানে প্রতিষ্ঠিত—প-সূ.।

উপবিচার করে। শ্রোত্র দ্বারা শব্দ শুনিয়া..., ঘ্রাণ দ্বারা আঘ্রাণ করিয়া... জিহ্বা দ্বারা রস আস্বাদন করিয়া, কায় দ্বারা স্প্রষ্টব্য স্পর্শ করিয়া..., মন দ্বারা ধর্ম জানিয়া... উপেক্ষা স্থানীয় ধর্ম উপবিচার করে। এইগুলিই ছয় সৌমনস্য উপবিচার, ছয় দৌর্মনস্য উপবিচার, ছয় উপেক্ষা-উপবিচার... কথিত হইয়াছে।

'এই ব্যক্তির চারি অধিষ্ঠান আছে, 'ইহা কথিত হইয়াছে। কী সম্পর্কে ইহা কথিত হইয়াছে? প্রজ্ঞা-অধিষ্ঠান, সত্য-অধিষ্ঠান, ত্যাগ-অধিষ্ঠান, উপশম-অধিষ্ঠান।... কথিত হইয়াছে।

'প্রজ্ঞালাভে প্রমত্ত থাকা উচিত নহে, সত্য রক্ষা করা উচিত, ত্যাগ অনুশীলন করা উচিত, শান্তিলাভ শিক্ষা করা উচিত' ইহা কথিত হইয়াছে। কী সম্পর্কে ইহা কথিত হইয়াছে? কিরূপে ভিক্ষু প্রজ্ঞালাভে প্রমত্ত থাকে না? এই ছয় ধাতু; যথা : পৃথিবীধাতু... বিজ্ঞানধাতু।

ভিক্ষু, পৃথিবীধাতু কী? পৃথিবীধাতু অধ্যাত্মও হইতে পারে, বাহ্য[১]ও হইতে পারে। অধ্যাত্ম পৃথিবীধাতু কী? পৃথিবীধাতু যাহা অধ্যাত্ম, প্রত্যাত্ম (ব্যক্তিগত), কক্‌খত (স্তব্ধ), খর (কর্কশ) এবং দেহান্তর্গত; যথা : কেশ, লোম, নখ, দন্ত, ত্বক, মাংস, স্নায়ু, অস্থি, অস্থি-মজ্জা, বৃক্ক, হৃদয়, যকৃৎ, ক্লোম, প্লীহা, ফুস্‌ফুস্, অন্ত্র, অন্ত্রগুণ, উদর, করীষ, অথবা এইরূপ যাহা কিছু অধ্যাত্ম, ব্যক্তিগত, কঠিন, কর্কশ ও দেহান্তর্গত। ভিক্ষু, ইহাকেই বলে অধ্যাত্ম পৃথিবীধাতু। যাহা অধ্যাত্ম পৃথিবীধাতু এবং যাহা বাহ্য পৃথিবীধাতু সমস্তই পৃথিবীধাতুই বটে। 'তাহা আমার নয়', 'আমি তাহা নহি', 'তাহা আমার আত্মা নহে' এইরূপে বিষয়টি যথার্থভাবে সম্যক প্রজ্ঞার দ্বারা দর্শন করা উচিত। এইরূপে যথার্থভাবে সম্যক প্রজ্ঞার দ্বারা তাহা দর্শন করিয়া পৃথিবীধাতু বিষয়ে চিত্ত নির্বেদ প্রাপ্ত হয়। পৃথিবীধাতুতে চিত্ত বীতরাগ হয়।

ভিক্ষু, আপধাতু কী? আপধাতু অধ্যাত্ম হইতে পারে, বাহ্যও হইতে পারে। ভিক্ষু, অধ্যাত্ম আপধাতু কী? যাহা অধ্যাত্ম, প্রত্যাত্ম, আপ নামীয়, আপ-অন্তর্গত ও দেহান্তর্গত; যথা : পিত্ত, শ্লেষ্মা, পুঁয, রক্ত, স্বেদ, মেদ, অশ্রু, বসা, ক্ষেড় (থুথু) সিকনী, লসিকা, মুত্র অথবা যাহা কিছু অধ্যাত্ম... সমস্তই আপধাতু বটে। 'তাহা আমার নয়'... চিত্ত বীতরাগ হয়।

ভিক্ষু, তেজধাতু কী? তেজধাতু অধ্যাত্ম হইতে পারে, বাহ্যও হইতে পারে। ভিক্ষু, অধ্যাত্ম তেজধাতু কী? যাহা অধ্যাত্ম, প্রত্যাত্ম (ব্যক্তিগত),

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[১]। মধ্যমনিকায় (প্রথম খণ্ড), পৃ. ২৫৮ দ্রষ্টব্য।

তেজনামীয়, তেজ-অন্তর্গত ও দেহান্তর্গত; যথা : যাহা সন্তপ্ত করে, জীর্ণ করে, পরিদাহন করে, যাহার দ্বারা অশিত, পীত, খাদিত আস্বাদিত সমস্তই সম্পূর্ণ পরিপক্ব হয় অথবা যাহা কিছু... উপাদত্ত (দেহান্তর্গত) ইহাকে অধ্যাত্ম তেজধাতু বলে।... তেজধাতু বটে... বীতরাগ হয়।

ভিক্ষু, বায়ুধাতু কী? বায়ুধাতু অধ্যাত্ম হইতে পারে, বাহ্যও হইতে পারে। অধ্যাত্ম বায়ুধাতু কী? যাহা অধ্যাত্ম, ব্যক্তিগত, বায়ু নামীয়, অধোগামী বায়ু, কুক্ষিগত বায়ু, কোষ্ঠাশ্রিত বায়ু, অঙ্গ-প্রত্যঙ্গ-বাহী বায়ু, বায়ু-অন্তর্গত ও দেহাধিকৃত; যথা : ঊর্ধ্বগামী বায়ু, শ্বাস-প্রশ্বাস অথবা যাহা কিছু অধ্যাত্ম... অন্তর্গত। ইহাকেই বলে... বায়ুধাতু বিষয়ে চিত্ত বীতরাগ হয়।

ভিক্ষু, আকাশধাতু কী? আকাশ ধাতু অধ্যাত্ম ইহাতে পারে, বাহ্যও হইতে পারে। ভিক্ষু, অধ্যাত্ম আকাশধাতু কী? যাহা অধ্যাত্ম... অন্তর্গত; যথা : কর্ণছিদ্র, নাসাছিদ্র, মুখদ্বার যাহার দ্বারা অশিত-পীত-খাদিত-স্বাদিত বস্তু সংস্থিত হয় আর যদ্বারা সেইগুলি অধভাগ দিয়া বাহির অথবা অন্য যাহা কিছু অধ্যাত্ম... উপাদত্ত... বীতরাগ হয়।

যে বিজ্ঞান অবশিষ্ট থাকে তাহা পরিশুদ্ধ পর্যবদাত, সেই বিজ্ঞানের দ্বারা তিনি কিছু জানিতে পারেন : সুখ জানেন, দুঃখ জানেন, না-দুঃখ-না সুখ জানেন। ভিক্ষু, সুখবেদনীয় স্পর্শের কারণে সুখবেদনা (সুখানুভূতি) উৎপন্ন হয়। তিনি সুখ বেদনা অনুভব করিয়া, 'সুখবেদনা অনুভব করিতেছি' বলিয়া জানেন, সেই সুখবেদনীয় স্পর্শের নিরোধ হইলে সুখবেদনীয় স্পর্শের কারণে যে সুখবেদনা উৎপন্ন হয়, তাহা নিরুদ্ধ হয়, উপশান্ত হয় বলিয়া জানেন। দুঃখবেদনা, না-দুঃখ-না-সুখ বেদনা সম্পর্কেও এইরূপ।

ভিক্ষু, যেমন দুইটি কাষ্ঠখণ্ডের সংঘর্ষে উত্তাপ উৎপন্ন হয়। তেজ (আলো) উৎপন্ন হয়, আবার দুইটি কাষ্ঠ পৃথক করিলে, নিক্ষেপ করিলে তদনুযায়ী উত্তাপ নিরুদ্ধ হয় ও ঠাণ্ডা ইহয়া যায়; ঠিক এইরূপে, ভিক্ষু, সুখবেদনীয় স্পর্শের কারণে... জানেন।

যে উপেক্ষা অবশিষ্ট থাকে তাহা পরিশুদ্ধ, পর্যবদাত, মৃদু, কর্মণ্য ও প্রভাস্বর। যেমন, ভিক্ষু, কোনো দক্ষ স্বর্ণকার বা স্বর্ণকার-অন্তেবাসী উল্কা প্রস্তুত করে, প্রস্তুত করিয়া উল্কা মুখ প্রজ্বলিত করিয়া সাঁড়াশী দ্বারা স্বর্ণখণ্ড ধরিয়া উল্কামুখে প্রক্ষেপ করে, তাহাতে মাঝে মাঝে ফুঁ দেয়, মাঝে মাঝে ফোঁস ফোঁস করিয়া জলসিঞ্চন করে, মাঝে মাঝে উত্তমরূপে পর্যবেক্ষণ করে, সেই স্বর্ণ পরিষ্কৃত, শুদ্ধ, মালিন্যশূন্য, মৃদু, কর্মণ্য ও প্রভাস্বর হয়, যাহাতে প্রয়োজন অনুযায়ী যথেচ্ছ অঙ্গুরীয়, কর্ণকুণ্ডলী, কণ্ঠহার ইত্যাদি বিভিন্ন

অলংকার প্রস্তুত করা যায়। এইরূপে, ভিক্ষু, যে উপেক্ষা অবশিষ্ট... প্রভাস্বর। তিনি ইহা প্রকৃষ্টভাবে জানেন : আমি যদি এই পরিশুদ্ধ, পর্যবদাত উপেক্ষাকে আকাশ-অনন্ত-আয়তনে কেন্দ্রীভূত করি এবং তদনুযায়ী চিত্তের ভাবনা করি, তাহা হইলে উপেক্ষা এইরূপে নিশ্রিত ও পুষ্ট হইয়া দীর্ঘকাল স্থায়ী হইবে। অনন্ত বিজ্ঞান-আয়তন, আকিঞ্চন-আয়তন, নৈবসংজ্ঞা-না-অসংজ্ঞায়তন সম্পর্কেও এইরূপ। তিনি ইহা প্রকৃষ্টরূপে জানেন : যদি আমি এই পরিশুদ্ধ, পর্যবদাত উপেক্ষাকে অনন্ত-আকাশ-আয়তনে কেন্দ্রীভূত করি, এবং তদনুযায়ী চিত্তের ভাবনা করি, তাহা হইলেও ইহা সংস্কৃত (সমবায়ে গঠিত, সুতরাং অনিত্য)। অনন্ত-বিজ্ঞান-আয়তন... নৈবসংজ্ঞা-না-অসংজ্ঞায়তন সম্পর্কেও এইরূপ। তিনি ভবের জন্য বা বিভবের জন্য প্রস্তুতি করেন না এবং চিন্তা করেন না, ভবের জন্য বা বিভবের জন্য অভিসংস্কার (প্রস্তুতি) ও চিন্তা না করার কারণে তিনি জগতে কিছুতে আসক্তি উৎপাদন করেন না, আসক্তি (উপাদান) না থাকিবার ফলে তাঁহার পরিত্রাস হয় না, অপরিত্রাসিত হইয়া তিনি ব্যক্তিগতভাবে পরিনির্বাণ লাভ করেন—জন্মবীজ ক্ষীণ হইয়াছে, ব্রহ্মচর্য ব্রত উদ্‌যাপিত হইয়াছে, করণীয় কার্য কৃত হইয়াছে, অতঃপর ইহলোকে আর আসিতে হইবে না বলিয়া তিনি প্রকৃষ্টরূপে জানেন। তিনি সুখ-বেদনা অনুভব করেন এবং তাহা অনিত্য বলিয়া প্রকৃষ্টরূপে জানেন, অনিবিষ্ট ও অনভিনন্দিত বলিয়া জানেন। দুঃখ-বেদনা, না-দুঃখ-না-সুখ-বেদনা সম্পর্কেও এইরূপ। তিনি বিসংযুক্ত হইয়া সুখবেদনা, দুঃখবেদনা, না-দুঃখ-না-সুখ বেদনা অনুভব করেন, তিনি কায় পর্যন্তিক বেদনা অনুভব করিয়া 'আমি কায়পর্যন্তিক বেদনা অনুভব করিতেছি' বলিয়া জানেন। তিনি জীবিতপর্যন্তিক বেদনা অনুভব করিয়া, 'আমি জীবিতপর্যন্তিক বেদনা অনুভব করিতেছি' বলিয়া জানেন, দেহান্তে জীবন-অবসান-হেতু সমস্ত আনন্দদায়ক বেদনা শীতলীভূত হইবে বলিয়া জানেন।

ভিক্ষু, যেমন তৈল এবং বর্তি উপাদান অবলম্বনে তৈলপ্রদীপ প্রজ্বলিত হয়, আবার তৈল এবং বর্তির অবসান-হেতু ও অন্য উপাদান আহরিত না হওয়ায় অনাহার বা ইন্ধনহীন হইয়া নিভিয়া যায়, এইরূপে ভিক্ষু,... শীতলীভূত হয় বলিয়া জানেন। সুতরাং তাহাতে সমন্বাগত ভিক্ষু পরম প্রজ্ঞা দ্বারা সমন্বাগত হন। ভিক্ষু, সর্বদুঃখক্ষয় জ্ঞান বিষয়ে ইহাই পরম আর্য প্রজ্ঞা। তাঁহার বিমুক্তি সত্যে স্থিত ও অকুপ্য। ভিক্ষু, তাহাই মৃষা (মিথ্যা) যাহা মিথ্যাধর্মী এবং তাহাই সত্য যাহা অমিথ্যাধর্মী ও নির্বাণ। সুতরাং এইরূপে সমন্বাগত ভিক্ষু পরম সত্য অধিষ্ঠান দ্বারা সমন্বাগত হন। ভিক্ষু, ইহাই পরম

আর্য সত্য যাহা অমিথ্যাধর্মী নির্বাণ। তাঁহার পূর্ব অবিদ্বানসুলভ উপধিগুলি সমাপ্তও বিনষ্ট হয়। সেইগুলি প্রহীন, উচ্ছিন্নমূল, শীর্ষহীন তালবৃক্ষ সদৃশ, পুনর্ভবরহিত হয়, ভবিষ্যতে উহাদের পুনর্ভবের সম্ভাবনা নাই। সুতরাং এইরূপে সমন্বাগত ভিক্ষু পরম ত্যাগ-অধিষ্ঠান দ্বারা সমন্বাগত হন। ভিক্ষু, ইহাই পরম আর্য ত্যাগ যাহা সর্ব উপধি-বিসর্জন। তাঁহার পূর্ব অবিদ্বানসুলভ অভিধ্যা, রাগযুক্ত ছন্দ (ইচ্ছা) ছিল। তাহা প্রহীন... পুনর্ভবের সম্ভাবনা নাই। তাঁহার পূর্ব অবিদ্বানসুলভ আঘাত, ব্যাপাদ বিদ্বেষ ছিল তাহা প্রহীন... সম্ভাবনা নাই। তাঁহার পূর্ব অবিদ্বানসুলভ অবিদ্যা সম্মোহ সম্প্রদোষ ছিল, তাহা... সম্ভাবনা নাই। সুতরাং এইরূপে সমন্বাগত ভিক্ষু পরম উপশম অধিষ্ঠান দ্বারা সমন্বাগত হন। ভিক্ষু, ইহাই পরম আর্য উপশম যাহা রাগাদ্বেষমোহের উপশম।

"প্রজ্ঞালাভে প্রমত্ত থাকা উচিত নয়, সত্য রক্ষা করা উচিত, ত্যাগ অনুশীলন করা উচিত এবং তাঁহার শান্তির জন্য শিক্ষালাভ করা উচিত" ইহা এই সম্পর্কেই কথিত হইয়াছে।

"যেখানে স্থিতি থাকে মান ও দম্ভ প্রবর্তিত হয় না, মান ও দম্ভ প্রবর্তিত না হইলে 'মুনি শান্ত' বলিয়া কথিত হয়," কী সম্পর্কে ইহা কথিত হইয়াছে? 'আমি ইহ' ইহা মনে করা হয়, 'আমি এই ইহ'... আমি হইব..., আমি হইব না... আমি রূপী হইব..., আমি অরূপী হইব, আমি সংজ্ঞী হইব.., আমি অসংজ্ঞী হইব... । আমি নৈবসংজ্ঞী-না-অসংজ্ঞী হইব..., ইহা মনে করা হয়। রোগ, গণ্ড, শল্য, ভিক্ষু, সর্বমনন অতিক্রম করিলে 'মুনি শান্ত' বলিয়া কথিত হয়। শান্ত মুনি উৎপন্ন হন না, উৎপাদন করেন না, কুপিত হন না, স্পৃহা করেন না, ভিক্ষু, তিনি জন্মগ্রহণ করেন না, অজাতের কিরূপে মৃত্যু হইবে? যাঁহার মৃত্যু নাই তিনি কিরূপে কুপিত হইবেন? অকুপিতে কিরূপে স্পৃহা থাকিবে? যেখানে স্থিতি থাকে... এই সম্পর্কেই তাহা বলা হইয়াছে।

ভিক্ষু, আমার দ্বারা সংক্ষিপ্তভাবে বর্ণিত এই ছয় ধাতুবিভঙ্গ ধারণ করো।

অতঃপর আয়ুষ্মান পুক্কুসাতি বলিলেন, বাস্তবিক, শাস্তা আমার নিকট আসিয়াছেন, সুগত... সম্যকসম্বুদ্ধ... ভাবিয়া আসন হইতে উঠিয়া একাংশে চীবর রাখিয়া ভগবানের পায়ে মস্তক নিপতিত করিয়া বলিলেন, "ভদন্ত, আমি মূর্খতা, মূঢ়তা ও অকুশলবশত অপরাধ করিয়াছি, আমি ভগবানকে 'বন্ধু' বলিয়া সম্বোধন করিয়াছিলাম, ভগবান আমার অপরাধকে অপরাধ বলিয়া স্বীকার করুন যাহাতে আমি ভবিষ্যতে সংযত হইতে পারি।"

"ভিক্ষু, যথার্থই তুমি মূর্খতা, মূঢ়তা ও অকুশলবশত অপরাধ করিয়াছ,

CHAPTER

1

Neuroanatomical Basis of Consciousness

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INTRODUCTION

Consciousness is of great importance to normal human quality of life. The nature of consciousness and the best way to understand and define it have long generated lively debate among scientists, philosophers, clinicians, and the general public. From a neurological perspective, consciousness is classically described as emerging from brain systems that make up the *content* of consciousness, regulated by distinct systems that control the *level* of consciousness (Plum and Posner, 1982).

The content of consciousness is the substrate upon which levels of consciousness act. This content includes all the various types of information processed by hierarchically organized sensory, motor, emotional, and memory systems in the brain (Figure 1.1). Much of neuroscience is dedicated to understanding the normal functioning of these systems. Selective deficits in contents of consciousness, such as loss of a portion of one's visual field, or sudden impairment in spoken language, are also the main subject matter of clinical neurology.

However, level of consciousness can affect all of these specific functions. The level of consciousness is controlled by specialized cortical and subcortical systems that determine the amount of alertness, attention, and awareness (mnemonic, AAA) (Blumenfeld, 2002).

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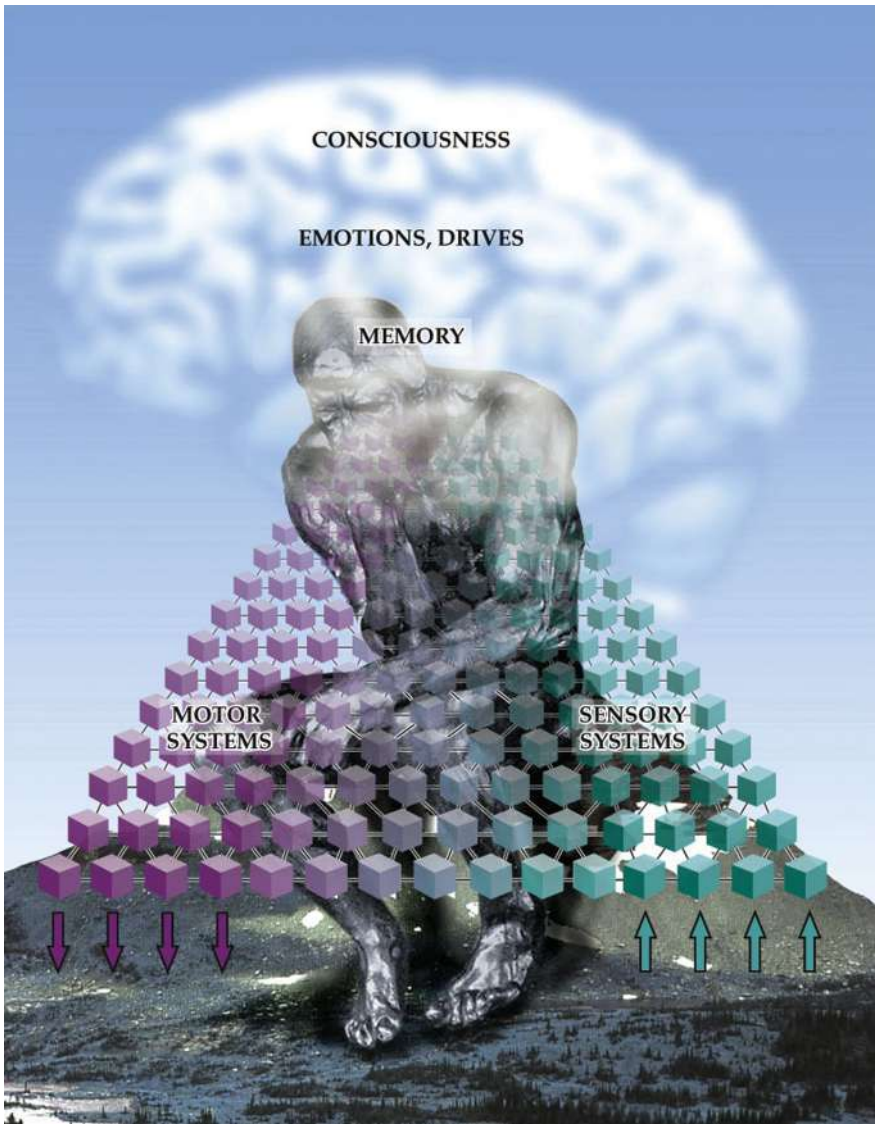

FIGURE 1.1 The content of consciousness. Parallel interconnected and hierarchically organized sensory and motor systems receive inputs, generate outputs, and perform internal processing on multiple levels, from relatively simple to highly abstract. Three additional special systems—mediating memory, emotions and drives, and consciousness itself—act on the other systems in a widely distributed manner, especially at the highest levels of processing. *Source: Modified with permission from Blumenfeld (2010).*

Basic alertness (arousal, wakefulness) is necessary for any meaningful responses to occur. Attention enables selective or sustained information to be processed. Finally, awareness is the ability to form experiences that can potentially be reported later. This chapter will review the neuroanatomical basis of brain systems that control the level of consciousness. In analogy with other cortical-subcortical systems such as the sensory, motor or limbic systems, the brain networks dedicated to regulating the level of consciousness can be referred to as the "consciousness system" (Blumenfeld, 2010, 2012). This chapter begins with an overview of the main cortical and subcortical structures that constitute the consciousness system. Next, the major subcortical networks that regulate level of consciousness are each discussed in turn, including the thalamus and subcortical arousal nuclei acting through multiple neurotransmitters (glutamate, acetylcholine, gamma amino butyric acid (GABA), norepinephrine, serotonin, dopamine, histamine, orexin) that arise from the upper brainstem, basal forebrain, and hypothalamus. The second half of the chapter reviews important cortical networks for controlling the level of alertness, attention, and awareness, including systems that select and encode conscious experiences into memories for subsequent report. This neuroanatomical review of the cortical and subcortical systems that control level of consciousness will serve as a general introduction to the normal functions as well as disorders of consciousness discussed in the remaining chapters in this book.

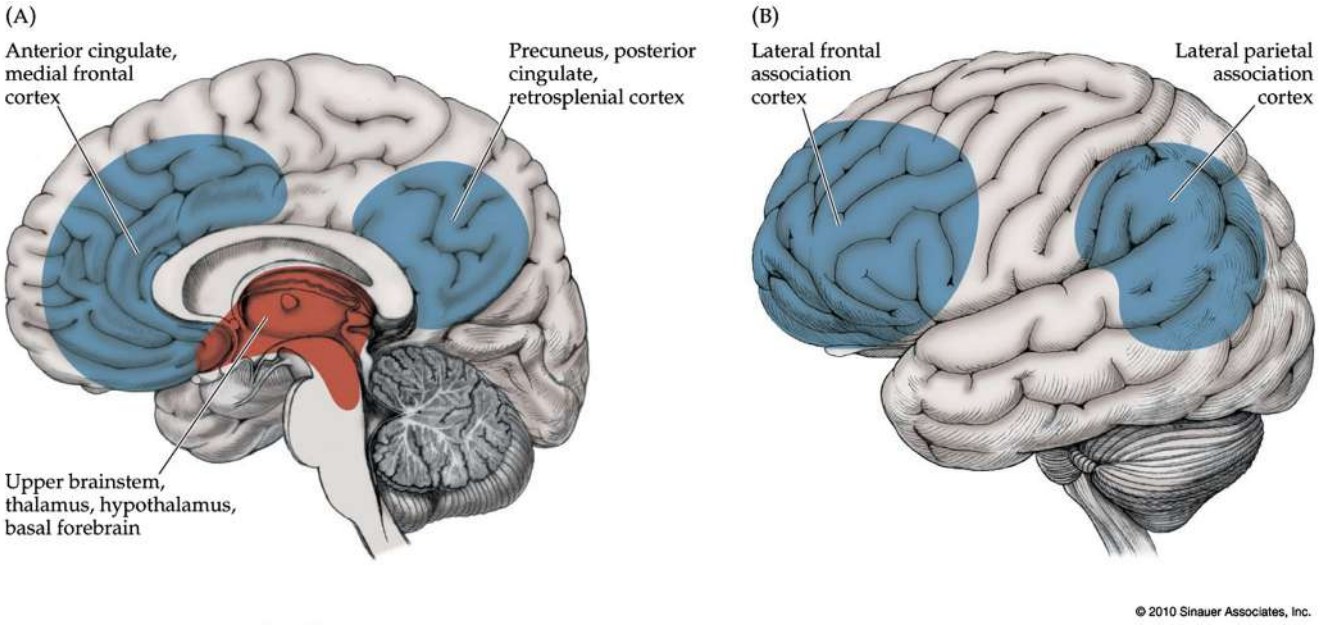

FIGURE 1.2 The consciousness system. Anatomical structures involved in regulating the level of consciousness, specifically controlling the level of alertness, attention and awareness. (A) Medial view showing cortical (blue) and subcortical (red) components of the consciousness system. (B) Lateral cortical components of the consciousness system. Note that other circuits not pictured here, such as the anterior insula, claustrum, basal ganglia, amygdala, and cerebellum, may also play a role in attention and other aspects of consciousness. *Source: Reproduced with permission from Blumenfeld (2010).*

THE CONSCIOUSNESS SYSTEM

The specialized brain networks controlling the level of consciousness can be referred to as the "consciousness system" (Blumenfeld, 2009, 2010) (Figure 1.2). It has long been recognized through studies based on human brain disorders (Penfield, 1950; Plum and Posner, 1972; Von Economo, 1930) as well as experimental animal models (Bremer, 1955; Moruzzi and Magoun, 1949; Steriade and McCarley, 2010) that the level of consciousness depends critically on both cortical and subcortical structures. Here we provide a brief overview of the cortical and subcortical networks comprising the consciousness system, which will be discussed in greater detail in the remaining sections of the chapter.

Cortical components of the consciousness system include the major regions of the higher-order "heteromodal" (Mesulam, 2000) association cortex (Figure 1.2; see also Figure 1.11). On the medial brain surface, important components are the medial frontal, anterior cingulate, posterior cingulate, and medial parietal (precuneus, retrosplenial) cortex (Figure 1.2A). On the lateral surface, major consciousness system networks include the lateral frontal, anterior insula, orbital frontal, and lateral temporal-parietal association cortex (Figure 1.2B).

It is important to recognize that individual components of the higher-order association cortex play important and well-studied roles in specific cognitive functions in the dominant and non-dominant hemispheres as described in the behavioral neurology literature (Heilman and Valenstein, 2003; Mesulam, 2000). Recently these same association cortex regions have also been described as participating in either so-called task-positive networks based on their activation during externally oriented attention (Asplund et al., 2010; Buschman and Miller, 2007; Dosenbach et al., 2007; Vanhaudenhuyse et al., 2011) or task-negative networks, also known as the "default mode" based on activity at rest (Fox et al., 2005; Raichle et al., 2001). Regardless of the heterogeneous functions of individual regions or networks, it is the *collective* activity of widespread areas of bilateral association cortex that determines the level of consciousness. Taken as a whole, the higher-order association cortex interacts with subcortical arousal systems (Steriade and McCarley, 2010) to exert powerful control over the overall level of arousal, attention, and awareness.

Subcortical components of the consciousness system include the upper brainstem activating systems, thalamus, hypothalamus, and basal forebrain (Figure 1.2A). It is likely that other subcortical structures (not shown) also participate, including portions of the basal ganglia, cerebellum, amygdala, and claustrum. Multiple parallel neurotransmitter systems participate in subcortical arousal including acetylcholine, glutamate, gamma amino butyric acid (GABA), norepinephrine, serotonin, dopamine, histamine, and orexin (Cooper et al., 2003; Saper et al., 2005; Steriade et al., 1997; Steriade and McCarley, 2010). Like the diverse cortical regions already discussed, these subcortical pathways

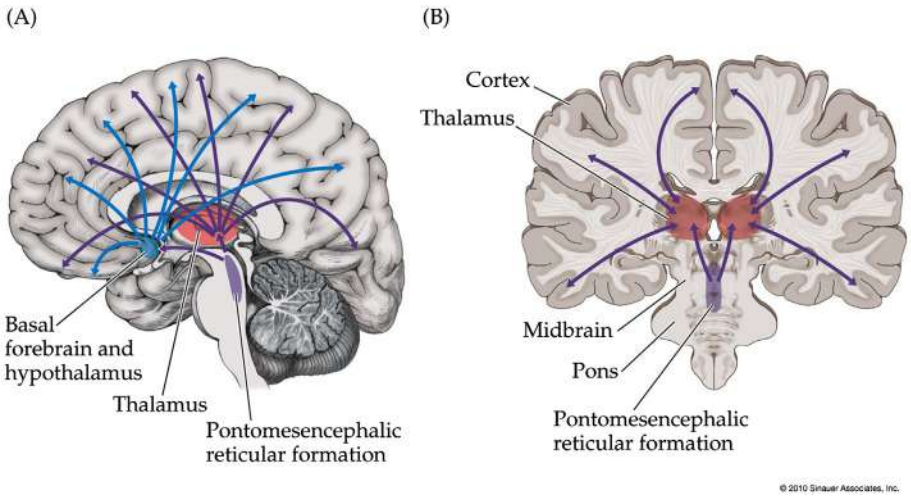

FIGURE 1.3 Arousal circuits of the pontomesencephalic reticular formation, thalamus, hypothalamus and basal forebrain. (A) Midsagittal view; (B) coronal view. Widespread projections to the cortex arise from outputs of the pontomesencephalic reticular formation relayed via the thalamic intralaminar nuclei, basal forebrain, and hypothalamus. *Source: Reproduced with permission from Blumenfeld (2010).*

each carry out individual roles, but it is the collective and parallel actions of all of these systems that together control the level of consciousness.

Understanding consciousness depends not only on neuroanatomy but also on neurophysiology. Although this chapter will focus on the "where" of consciousness, equally important is "how" these networks interact to form consciousness. Recent proposed physiological mechanisms for consciousness include synchronized oscillations (Buzsaki and Wang, 2012; Llinás and Paré, 1997; Singer, 1998), slow cortical potentials (Li et al., 2014), connectivity (Boly et al., 2011; Rosanova et al., 2012; Rubinov and Sporns, 2010), information integration (Tononi, 2005; Tononi and Koch, 2008), population neuroenergetics (Shulman et al., 2003), and recurrent or global neuronal processing (Dehaene et al., 1998; Lamme and Roelfsema, 2000; Sergent and Dehaene, 2004) among others. Much additional work is needed before the physiological mechanisms of consciousness are more definitely known. By contrast, when it comes to neuroanatomy, the past century of research has at least led to a basic understanding of the most important brain structures contributing to consciousness. We now turn in greater detail to these major cortical and subcortical networks that constitute the consciousness system.

SUBCORTICAL NETWORKS AND CONSCIOUSNESS

The main subcortical components of the consciousness system include the midbrain and upper pons, thalamus, hypothalamus, and basal forebrain (Figure 1.2). These structures contribute importantly to maintaining alertness and arousal. Attention and awareness are also facilitated by the same midline arousal systems, as well as by other subcortical networks including the superior colliculi, cerebellum, amygdala, basal ganglia, claustrum, and thalamic reticular nucleus (Crick and Koch, 2005; Dreher and Grafman, 2002; Krauzlis et al., 2013; O'Halloran et al., 2012; Zikopoulos and Barbas, 2012).

In terms of alertness and arousal, much has been learned about the basic anatomy of consciousness by understanding which brain lesions can cause coma. Coma is as a state of unarousable unresponsiveness in which the eyes are closed and no purposeful responses can be elicited (Fisher, 1969; Plum and Posner, 1972). Coma occurs either through bilateral damage to widespread cortical areas, or via lesions in a core set of structures lying in upper brainstem and medial diencephalon. These critical subcortical arousal structures were initially identified based on strokes and other localized disorders in human patients (Penfield, 1950; Plum and Posner, 1972; Von Economo, 1930) as well as lesion, disconnection, and stimulation experiments performed in animal models (Bremer, 1955; Moruzzi and Magoun, 1949; Steriade and McCarley, 2010). In the brainstem, the subcortical arousal systems begin in the upper pons and extend to the midbrain. Lesions in this small but critical region of the upper pons and midbrain produce profound coma, whereas lesions in the lower pons or medulla do not typically disrupt consciousness (Figure 1.3). The core brainstem arousal systems lie in the tegmentum and include a variety of nuclei embedded within the brainstem reticular formation. The tegmentum is sandwiched between the more ventral brainstem basis—containing ascending and descending white matter pathways; and the more

TABLE 1.1 Widespread Projection Systems in the Nervous System

Projection system	Location(s) of cell bodies	Main target(s)	Neurotransmitter receptor(s)[a,b]	Function(s)[c]
Reticular formation	Midbrain and rostral pons	Thalamic intralaminar nuclei, hypothalamus, basal forebrain	Unknown (glutamate?)[d]	Alertness
Intralaminar nuclei	Thalamic intralaminar nuclei	Cortex, striatum	(Glutamate?)	Alertness
Midline thalamic nuclei	Midline thalamic nuclei	Cortex	(Glutamate?)	Alertness
Norepinephrine	Pons: locus ceruleus and lateral tegmental area	Entire CNS	α_{1A-D}, α_{2A-D}, β_{1-3}	Alertness, attention, mood elevation
Dopamine	Midbrain: substantia nigra pars compacta and ventral tegmental area	Striatum, limbic cortex, amygdala, nucleus accumbens, prefrontal cortex	D_{1-5}	Movements, initiative, working memory
Serotonin	Midbrain, pons, and medulla: raphe nuclei	Entire CNS	5-HT_{1A-F}, 5-HT_{2A-C}, 5-HT_{3-7}	Alertness, mood elevation, breathing control
Histamine	Hypothalamus: tubero-mammillary nucleus; midbrain: reticular formation	Entire brain	H_{1-4}	Alertness
Orexin (hypocretin)	Posterior lateral hypothalamus	Entire brain	OX_1, OX_2	Alertness, food intake
Acetylcholine	Basal forebrain: nucleus basalis, medial septal nucleus, and nucleus of diagonal band	Cerebral cortex including hippocampus	Muscarinic (M_{1-5}), nicotinic subtypes	Alertness, memory
	Pontomesencephalic region: pedunculopontine nucleus and laterodorsal tegmental nucleus	Thalamus, cerebellum, pons, medulla	Muscarinic (M_{1-5}), nicotinic subtypes	Alertness, memory

[a]*Many of the neurons releasing the neuromodulatory transmitters listed here also release a variety of peptides, which are likely to play a neuromodulatory role as well.*
[b]*Additional receptor subtypes are constantly being added.*
[c]*Functions listed are highly simplified here; see references at the end of this chapter for additional details.*
[d]*Entries in parenthesis with question mark are uncertain.*
Source: Modified with permission from Blumenfeld (2010).

dorsal tectum—lying dorsal to the cerebral aqueduct or fourth ventricle. Lesions outside the brainstem tegmentum in the basis or tectum do not produce coma. Bilateral lesions of the thalamus, particularly in the intralaminar and midline thalamic nuclei, can also produce profound suppression of arousal.

Subsequent work has revealed that the subcortical arousal systems consist of multiple parallel neurotransmitter systems and pathways (Figure 1.3; Table 1.1). Unlike most pathways in the nervous system which project to relatively narrow target regions, the subcortical arousal systems belong to a set of widespread projecting systems (Table 1.1) that reach many structures or even the entire nervous system. Interestingly the projection systems arising from the upper brainstem including the midbrain and upper pons (pontomesencephalic reticular formation; Figure 1.3) tend to project upward to the cortex, diencephalon, and basal forebrain while those in the lower pons and medulla project downward to the brainstem, cerebellum, and spinal cord. The upward projecting systems were originally called the "ascending reticular activating system" (ARAS) (Moruzzi and Magoun, 1949) recognizing their important role in arousal. Although the term "ARAS" is still occasionally used, in reality these arousal systems arise from a variety of specific nuclei (Table 1.1) rather than from what was formerly considered a single diffusely organized system.

The subcortical arousal systems in the midbrain and upper pons have three main targets (Figure 1.3): (i) Putative glutamatergic neurons from the reticular formation and cholinergic neurons from the pedunculopontine tegmental nucleus and laterodorsal tegmental nucleus (LDT) project mainly to the thalamus, particularly to the thalamic intralaminar nuclei which, in turn, increase cortical arousal. (ii) Other neurons project to the nucleus basalis and hypothalamus, which again relay arousal influences to the cortex. (iii) Finally, the monaminergic neurotransmitter systems (norepinephrine, dopamine, serotonin; not shown in Figure 1.3) project directly to the entire forebrain including the cortex and subcortical structures.

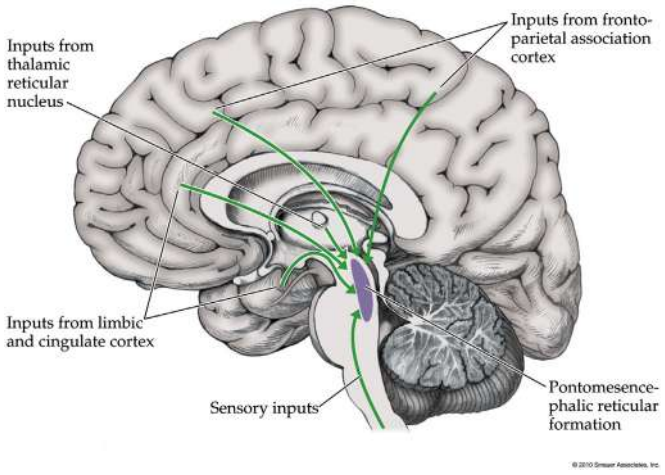
Inputs from thalamic reticular nucleus
Inputs from fronto-parietal association cortex
Inputs from limbic and cingulate cortex
Sensory inputs
Pontomesence-phalic reticular formation

FIGURE 1.4 Major inputs to the pontomesencephalic reticular formation and related structures. *Source: Reproduced with permission from Blumenfeld (2010).*

In addition to these ascending connections, the subcortical arousal systems are also highly interconnected and strongly influence each other's function through multiple connections within and between the brainstem, thalamus, hypothalamus, and basal forebrain.

The upper brainstem arousal systems are influenced by a variety of inputs including numerous regions of the association cortex and limbic cortex, as well as sensory pathways such as the anterolateral pain transmission pathways (Figure 1.4). Inhibitory influences arise from the thalamic reticular nucleus (not to be confused with the reticular formation) as well as other GABAergic inputs (Parent and Steriade, 1981, 1984; Ropert and Steriade, 1981). The arousal systems are also strongly regulated by brainstem and hypothalamic circuits controlling circadian sleep rhythms (Saper et al., 2005, 2010).

The subcortical arousal systems will now each be discussed in greater detail to more fully appreciate the functional anatomy of these complex parallel arousal systems and their contributions to consciousness. It should be noted that, unlike gross lesions of the brainstem-diencephalic arousal systems, lesions or pharmacological blockade of the individual projecting neurotransmitter systems do not cause coma. Blockade of some neurotransmitters, especially acetylcholine or histamine, produces severe confusion and drowsiness, but not coma. Thus, the normal awake, conscious state does not depend on a single projection system, but rather on the parallel action of multiple anatomical and neurotransmitter systems acting together (Table 1.1). After discussing each of the major subcortical arousal systems, emphasizing their role in maintaining the alert state, we will then briefly discuss their role together with other subcortical structures (tectal region, basal ganglia, claustrum, cerebellum) in attention and awareness.

The Thalamus and Consciousness

Nearly all information destined for the cortex first reaches the thalamus. The thalamus transmits this information and then receives an even greater number of reciprocal connections back from the cortex. Therefore the thalamus plays a key role in all aspects of forebrain function including consciousness. The thalamus relays the content of consciousness, and also controls the level of consciousness through specialized circuits that regulate the level of arousal and are crucial for selective attention.

Organization of the thalamus can be described based on regions or based on projections. The regional organization of the thalamus divides the thalamic subnuclei proceeding from lateral to medial (Figure 1.5) into the thalamic reticular nucleus located most laterally, followed by the lateral nuclear group which contains the largest number of thalamic relay nuclei (Table 1.2). Continuing medially, next comes the Y-shaped white matter internal medullary lamina which separates the lateral, anterior, and medial nuclear groups from each other (Figure 1.5). Embedded within the internal medullary lamina lie the intralaminar nuclei. Finally a thin layer of midline thalamic nuclei are located most medially, adjacent to the third ventricle (Figure 1.5).

Projection patterns can also be used to classify the thalamic subnuclei (Table 1.2). Some, such as the ventral posterior lateral nucleus, a somatosensory relay in the lateral thalamus, project to a relatively localized region of cortex, and are referred to as specific relay nuclei. Others, such as the thalamic intralaminar nuclei, have more widespread projections to many cortical areas, and are called diffusely or widely projecting ("nonspecific") nuclei.

The specific thalamic relay nuclei communicate with the cortex regarding each sensory and motor function, and are therefore responsible for all the individual contents of consciousness. On the other hand, the widely projecting thalamic nuclei influence the overall level of cortical arousal, and therefore control the level of consciousness. The rostral intralaminar nuclei (central lateral, paracentral, central medial nuclei; Table 1.2) and midline thalamic nuclei are thought to be particularly important for activating the cortex (Figure 1.3). As was already discussed, the intralaminar thalamus plays a key role in transmitting arousal influences from the midbrain and upper pontine cholinergic and glutamatergic systems to the cortex.

The thalamic reticular nucleus forms a thin shell of predominantly GABAergic inhibitory neurons on the lateral thalamus (Figure 1.5). As axons traverse this nucleus traveling from thalamus to cortex or from cortex back to thalamus they give off collateral

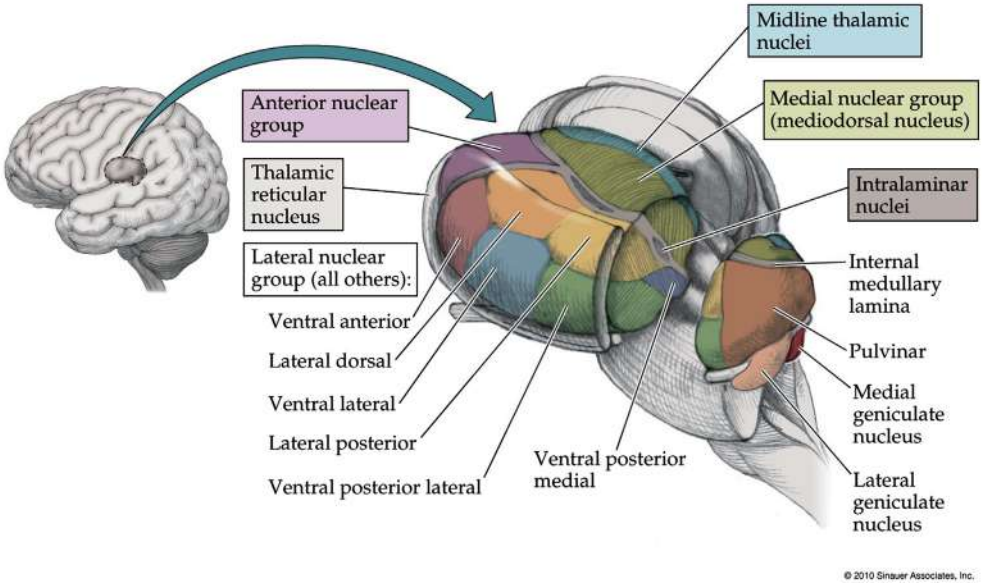

FIGURE 1.5 The thalamus. Main nuclear divisions and nuclei are shown (see also Table 1.2). The posterior portion of the reticular nucleus has been removed. *Source: Reproduced with permission from Blumenfeld (2010).*

branches to the thalamic reticular neurons. The thalamic reticular neurons, in turn, project to the thalamus and inhibit the specific thalamocortical neurons corresponding to individual corticothalamic loops. The reciprocal connections between thalamic relay nuclei and the thalamic reticular nucleus are thought to play an important role in generating corticothalamic rhythms during normal sleep and waking activity, as well as in pathological rhythms such as epilepsy (McCormick, 2002; McCormick and Bal, 1997; McCormick and Contreras, 2001; Steriade et al., 1993b). These physiological rhythms are crucial for regulating the level of consciousness. In addition, the thalamic reticular nucleus influences arousal through long-range inhibitory projections to the pontomesencephalic reticular formation (Parent and Steriade, 1984). Selective attention may also be mediated through the particular arrangement of reticular thalamic neurons and their directed inhibitory projections to the thalamus, which are capable of generating an inhibitory surround around a "searchlight" of focused attention in a narrow band of thalamocortical channels (Crick, 1984; Mayo, 2009; Pinault, 2004).

Glutamatergic and Related Arousal Systems

Glutamate is the most prevalent excitatory neurotransmitter of the central nervous system. For many of the arousal systems the most likely neurotransmitter is glutamate, although it has not been identified with certainty (Steriade and McCarley, 2010). Arousal system pathways probably mediated by glutamate include those arising from the midbrain and upper pontine reticular formation that project to the thalamus and basal forebrain (Steriade, 2004; Steriade et al., 1993a), as well as the widespread projections from the thalamic intralaminar nuclei to the cortex (Figure 1.3). It is not known whether other excitatory amino acid neurotransmitters such as aspartate might also play a significant role in arousal.

Cholinergic Arousal Systems

Acetylcholine is the major neurotransmitter of the peripheral nervous system, but in the central nervous system it has a more neuromodulatory function, where its role in arousal has been studied extensively. The two main sources of cholinergic projections neurons in the central nervous system lie in the brainstem pontomesencephalic reticular formation and in the basal forebrain (Figure 1.6; Table 1.1). At the junction of the midbrain and pons, the pedunculopontine nucleus is located in the lateral reticular formation, while the laterodorsal tegmental nucleus lies in the periaqueductal gray (Mesulam et al., 1983). The pedunculopontine nucleus stretches from the caudal midbrain substantia nigra *pars* reticulata into the rostral pons towards the superior cerebellar peduncle (Mena-Segovia et al., 2009; Rye et al., 1987). The nucleus has a gradient of increasing cholinergic and decreasing GABAergic neurons as it extends caudally, and also contains glutamatergic neurons (Wang and Morales, 2009). Cholinergic neurons from these brainstem nuclei project to the thalamus, including the intralaminar nuclei, playing an important role in arousal. Brainstem cholinergic

TABLE 1.2 Major Thalamic Nuclei

Nuclei[a]	Main inputs[b]	Main outputs	Diffuseness of projections to cortex[c]	Proposed functions
RELAY NUCLEI				
Lateral nuclear group				
Ventral posterior lateral nucleus	Medial lemniscus, spinothalamic tract	Somatosensory cortex	+	Relays somatosensory spinal inputs to cortex
Ventral posteromedial nucleus	Trigeminal lemniscus, trigeminothalamic tract, taste inputs	Somatosensory and taste cortex	+	Relays somatosensory cranial nerve inputs and taste to cortex
Lateral geniculate nucleus	Retina	Primary visual cortex	+	Relays visual inputs to cortex
Medial geniculate nucleus	Inferior colliculus	Primary auditory cortex	+	Relays auditory inputs to cortex
Ventral lateral nucleus	Internal globus pallidus, deep cerebellar nuclei, substantia nigra pars reticulata	Motor, premotor, and supplementary motor cortex	+	Relays basal ganglia and cerebellar inputs to cortex
Ventral anterior nucleus	Substantia nigra pars reticulata, internal globus pallidus, deep cerebellar nuclei	Widespread to frontal lobe, including prefrontal, premotor, and supplementary motor cortex	+++	Relays basal ganglia and cerebellar inputs to cortex
Pulvinar	Tectum (extrageniculate visual pathway), other sensory inputs	Parietotemporo-occipital association cortex	++	Behavioral orientation toward relevant visual and other stimuli
Lateral dorsal nucleus	See anterior nucleus	–	++	Functions with anterior nuclei
Lateral posterior nucleus	See pulvinar	–	++	Functions with pulvinar
Ventral medial nucleus	Midbrain reticular formation	Widespread to cortex	+++	May help maintain alert, conscious state
Medial nuclear group				
Mediodorsal nucleus (MD)	Amygdala, olfactory cortex, limbic basal ganglia	Frontal cortex	++	Limbic pathways, major relay to frontal cortex
Anterior nuclear group				
Anterior nucleus	Mammillary body, hippocampal formation	Cingulate gyrus	+	Limbic pathways
Midline thalamic nuclei				
Paraventricular, parataenial, interanteromedial, intermediodorsal, rhomboid, reuniens (medial ventral)	Hypothalamus, basal forebrain, amygdala, hippocampus	Amygdala, hippocampus, limbic cortex	++	Limbic pathways
INTRALAMINAR NUCLEI				
Rostral intralaminar nuclei				
Central medial nucleus Paracentral nucleus Central lateral nucleus	Deep cerebellar nuclei, globus pallidus, brainstem ascending reticular activating systems (ARAS), sensory pathways	Cerebral cortex, striatum	+++	Maintain alert consciousness; motor relay for basal ganglia and cerebellum
Caudal intralaminar nuclei				
Centromedian nucleus Parafascicular nucleus	Globus pallidus, ARAS, sensory pathways	Striatum, cerebral cortex	+++	Motor relay for basal ganglia
RETICULAR NUCLEUS				
Reticular nucleus	Cerebral cortex, thalamic relay and intralaminar nuclei, ARAS	Thalamic relay and intralaminar nuclei, ARAS	None	Regulates state of other thalamic nuclei

[a] *Some additional, smaller nuclei have not been included here.*
[b] *In addition to the inputs listed, all thalamic nuclei receive reciprocal inputs from the cortex and from the thalamic reticular nucleus. Modulatory cholinergic, noradrenergic, serotonergic, and histaminergic inputs also reach most thalamic nuclei.*
[c] *+ represents least diffuse (specific thalamic relay nuclei); ++ represents moderately diffuse; +++ represents most diffuse.*
Source: Modified with permission from Blumenfeld (2010).

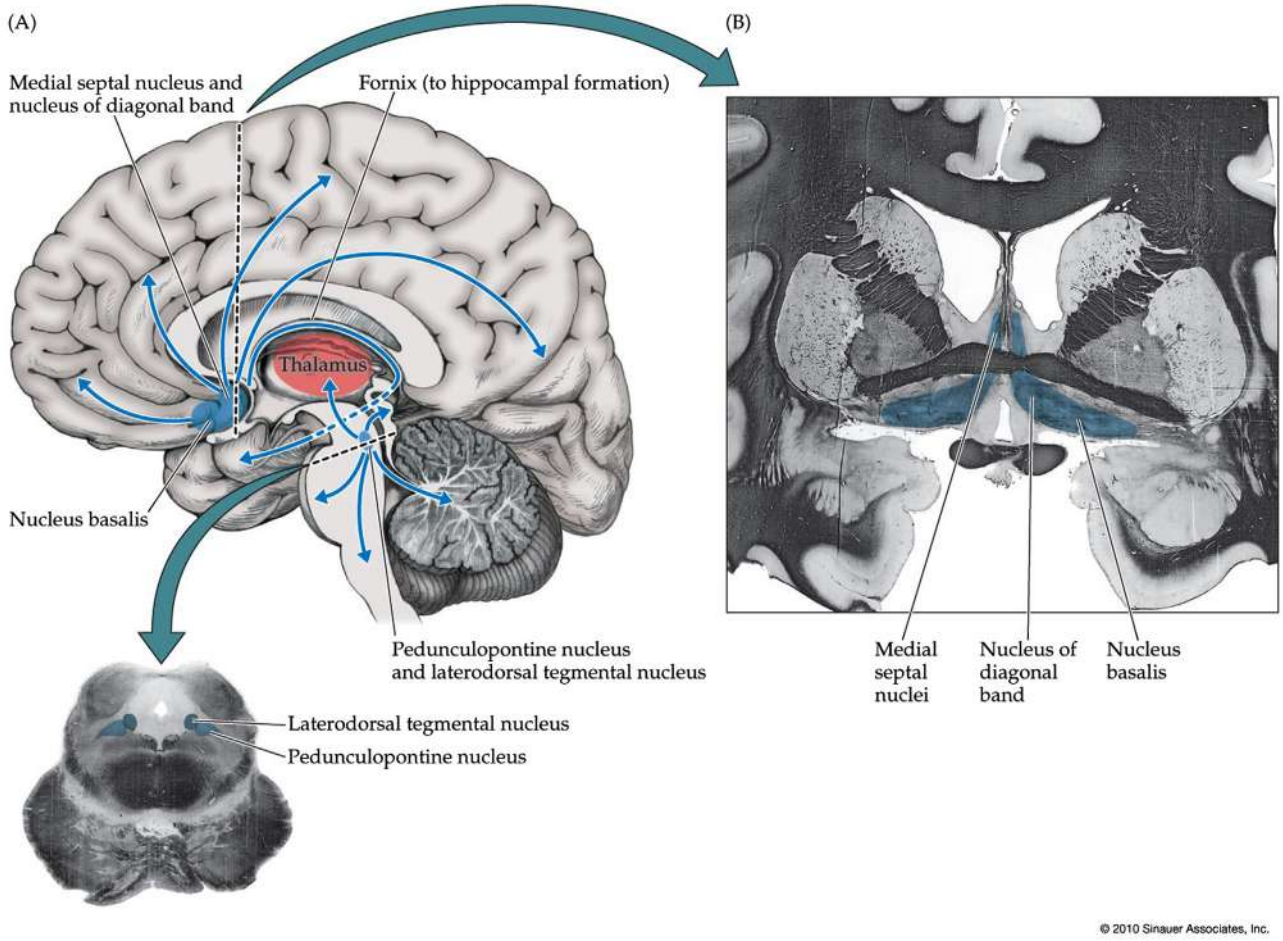

FIGURE 1.6 Cholinergic projection systems. (A) Overview and inset showing axial section through caudal midbrain. (B) Coronal section through basal forebrain. See also Table 1.1. *Source: Reproduced with permission from Blumenfeld (2010).*

arousal is thought to act synergistically with non-cholinergic putative glutamatergic pontomesencephalic neurons that project to intralaminar thalamus and basal forebrain (Figure 1.3) (Rasmusson et al., 1994, 1996; Steriade, 2004; Steriade et al., 1993a). In sleep, pontogeniculate waves arise from cholinergic brainstem neurons projecting to thalamocortical neurons in the lateral geniculate nucleus (Steriade et al., 1989, 1990). The pedunculopontine nucleus also has numerous ascending and descending motor projections and is involved in controlling locomotion (Inglis and Winn, 1995).

Interestingly, the brainstem has very few direct cholinergic projections to the cortex and nearly all facilitatory effects of the brainstem cholinergic systems on cortex are mediated via the thalamus (Beninato and Spencer, 1987; Cornwall et al., 1990; Hallanger et al., 1987; Hallanger and Wainer, 1988; Heckers et al., 1992; Jones and Webster, 1988; Satoh and Fibiger, 1986). The major source of cholinergic input to the cortex is the basal forebrain (Figure 1.6; Table 1.1). Cholinergic neurons in the nucleus basalis of Meynert and surrounding regions (substantia innominata, globus pallidus, and preoptic magnocellular nucleus) not only project to almost the entire neocortex (Mesulam et al., 1983; Rye et al., 1984) but also innervate some nuclei in the thalamus (reticular thalamic, mediodorsal, anteroventral/anteromedial, and ventromedial nuclei) (Heckers et al., 1992; Parent et al., 1988; Steriade et al., 1987). The hippocampal archicortex, however, receives cholinergic inputs mainly from the medial septal nuclei and nucleus of the diagonal band of Broca (Rye et al., 1984). Additional cholinergic neurons lie in the medial habenula, and short-range cholinergic neurons are present in the striatum and to a more limited extent within the cortex itself. Like the brainstem cholinergic nuclei, the basal forebrain contains both cholinergic and non-cholinergic neurons, including GABA and glutamate as transmitters among others (Brashear et al., 1986; Alvaro Duque et al., 2007).

The brainstem and basal forebrain cholinergic systems work together to abolish cortical slow wave

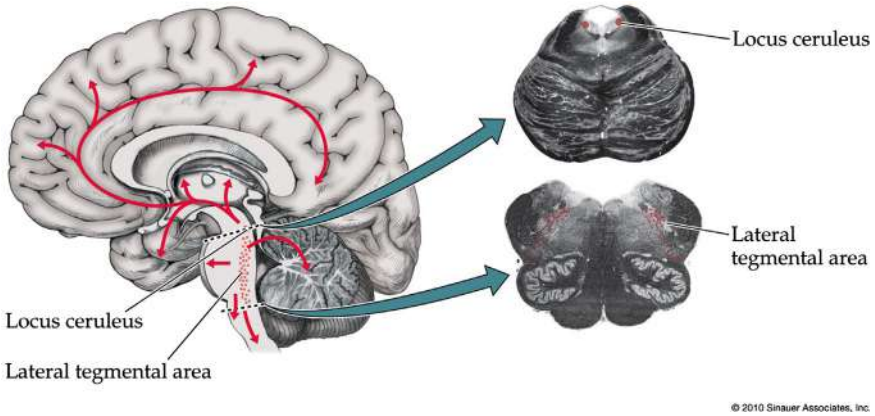

FIGURE 1.7 Noradrenergic projection systems. See also Table 1.1. *Source: Reproduced with permission from Blumenfeld (2010).*

activity and promote an alert state (Dringenberg and Olmstead, 2003; Steriade, 2004). Cholinergic arousal in the central nervous system is mediated predominantly by muscarinic acetylcholine receptors, although nicotinic receptors may also play an important role in arousal and attention (Bloem et al., 2014). As would be expected from the connections of cholinergic neurons described here, pharmacological blockade of central cholinergic neurotransmission produces an acute state of delirium and memory loss. However, despite the importance of acetylcholine in consciousness, selective damage to cholinergic neurotransmission does not produce coma (Blanco-Centurion et al., 2006, 2007; Buzsaki et al., 1988; Fuller et al., 2011), presumably because of the multiple parallel neurotransmitter systems participating in consciousness as already discussed.

GABAergic Arousal Systems

Found in local inhibitory interneurons throughout the cortex and subcortical structures, GABA is the most prevalent inhibitory neurotransmitter in the central nervous system and plays a major role in regulating arousal. Several long-range GABAergic projection systems also contribute to controlling arousal. Some GABAergic neurons in the basal forebrain are thought to promote arousal because these inhibitory neurons in turn project to cortical inhibitory interneurons (Freund and Meskenaite, 1992). However, the overall effects of basal forebrain GABAergic neurons on arousal may be heterogeneous because of variable firing patterns with respect to cortical activation and sleep-wake cycles (Hassani et al., 2009; Jones, 2004; Manns et al., 2000); and because parvalbumin-containing GABAergic neurons are related to cortical desynchrony whereas neuropeptide Y-containing neurons may have the opposite effect (Alvaro Duque et al., 2000, 2007).

Other important long-range GABAergic projections mainly inhibit arousal. These include neurons in the ventral lateral preoptic nucleus, which have widespread inhibitory projections to virtually all subcortical arousal systems (Saper et al., 2010); lateral septal GABAergic neurons thought to inhibit the basal forebrain and hypothalamus (Mesulam and Mufson, 1984; Varoqueaux and Poulain, 1999); and the thalamic reticular nucleus which contains GABAergic neurons projecting both to the remainder of the thalamus and to the brainstem reticular formation (Parent and Steriade, 1984; Steriade et al., 1984). In addition, GABAergic neurons in the globus pallidus internal segment inhibit regions of the thalamus including the intralaminar nuclei. It has been proposed that paradoxical arousal effects of GABA agonists such as zolpidem in minimally conscious state, or benzodiazepines in catatonia may occur when these agents inhibit the globus pallidus, thereby removing tonic inhibition of the intralaminar thalamus (Brown et al., 2010; Giacino et al., 2014). Activation of these multiple GABAergic inhibitory projections converging on the subcortical arousal systems has also been proposed as the mechanism for loss of consciousness in partial seizures (Blumenfeld, 2012; Englot and Blumenfeld, 2009).

Noradrenergic Arousal Systems

Norepinephrine (noradrenaline)-containing neurons are located in the locus ceruleus in the rostral pons adjacent to the fourth ventricle, as well as in the nearby lateral tegmental area extending into the more caudal pons and medulla (Figure 1.7; Table 1.1). Ascending noradrenergic projections reach the cortex, thalamus and hypothalamus (Foote et al., 1983; Morrison et al., 1981; Pickel et al., 1974) to regulate sleep-wake cycles, attention, and mood, while descending projections to the brainstem, cerebellum, and spinal cord modulate autonomic function and gating of pain. Many attention-enhancing drugs such as amphetamines augment noradrenergic function. Norepinephrine is thought to

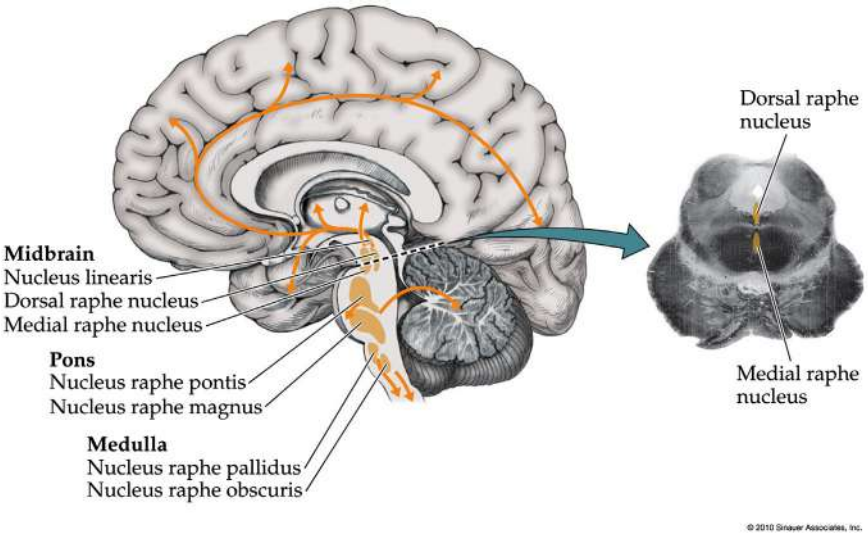

FIGURE 1.8 Serotonergic projections systems. See also Table 1.1. *Source: Reproduced with permission from Blumenfeld (2010).*

play an important role in promoting arousal (Berridge, 2008; Berridge et al., 2012; Constantinople and Bruno, 2011). For example, selective α-2 agonists such as clonidine or the anesthetic agent dexmedetomidine markedly depress arousal possibly by inhibiting locus ceruleus neurons (Correa-Sales et al., 1992; De Sarro et al., 1987; Scheinin and Schwinn, 1992). However, selective removal or blockade of noradrenergic neurons affects arousal but does not produce coma (Berridge et al., 1993; Blanco-Centurion et al., 2004, 2007; Cirelli and Tononi, 2004; Hunsley and Palmiter, 2003) again reinforcing the notion of multiple parallel systems promoting consciousness.

Serotoninergic Arousal Systems

Serotonergic neurons are found predominantly in the midline raphe nuclei of the midbrain, pons, and medulla (Figure 1.8; Table 1.1). The more rostral serotonergic neurons in the midbrain and upper pontine raphe nuclei project to the entire forebrain, participating in sleep-wake regulation; dysfunction of serotonergic systems is thought to play a role in a number of psychiatric disorders including depression, anxiety, obsessive-compulsive disorder, aggressive behavior, and eating disorders. More caudal serotonergic neurons in the pons and medulla are important for modulation of breathing, pain, temperature control, cardiovascular, and motor function.

The most important rostral raphe nuclei participating in arousal are the dorsal raphe and median raphe (Jacobs and Azmitia, 1992; Wiklund et al., 1981). The role of serotonergic neurons in arousal is complex, possibly because the large diversity of serotonin receptors (Hannon and Hoyer, 2008) leads to effects that either promote or inhibit arousal in different brain regions (Dugovic et al., 1989; Dzoljic et al., 1992; Kumar et al., 2007; Lemoine et al., 2007; Leonard and Llinás, 1994; Luebke et al., 1992; Monckton and McCormick, 2002; Muraki et al., 2004; Rogawski and Aghajanian, 1980). Rostral brainstem serotonergic neurons have been proposed to promote arousal in response to hypoventilation and increased carbon dioxide levels, perhaps playing an important role in preventing sudden infant death syndrome and sudden unexplained death in epilepsy (Buchanan and Richerson, 2010; Kinney et al., 2009; Richerson and Buchanan, 2011; Sowers et al., 2013).

Dopaminergic Arousal Systems

Most dopaminergic neurons are located in the ventral midbrain, either in the substantia nigra pars compacta or in the adjacent ventral tegmental area (Figure 1.9; Table 1.1). These mesencephalic nuclei give rise to the following three ascending dopaminergic projection systems: (i) the mesostriatal (nigrostriatal) pathway projects from the substantia nigra to the caudate and putamen (Matsuda et al., 2009); (ii) the mesolimbic pathway arises mainly from the ventral tegmental area and projects to limbic structures including the medial temporal lobe, amygdala, cingulate gyrus, septal nuclei, and nucleus accumbens (Fallon, 1981; Oades and Halliday, 1987); (iii) the mesocortical pathway arises mainly from the ventral tegmental area as well as scattered neurons in the vicinity of the substantia nigra and ventral periaqueductal gray, projecting to the prefrontal cortex (Figure 1.9) as well as to the thalamus (Garcia-Cabezas et al., 2009; Groenewegen, 1988; Lu et al., 2006; Sanchez-Gonzalez et al., 2005). Dopaminergic neurons

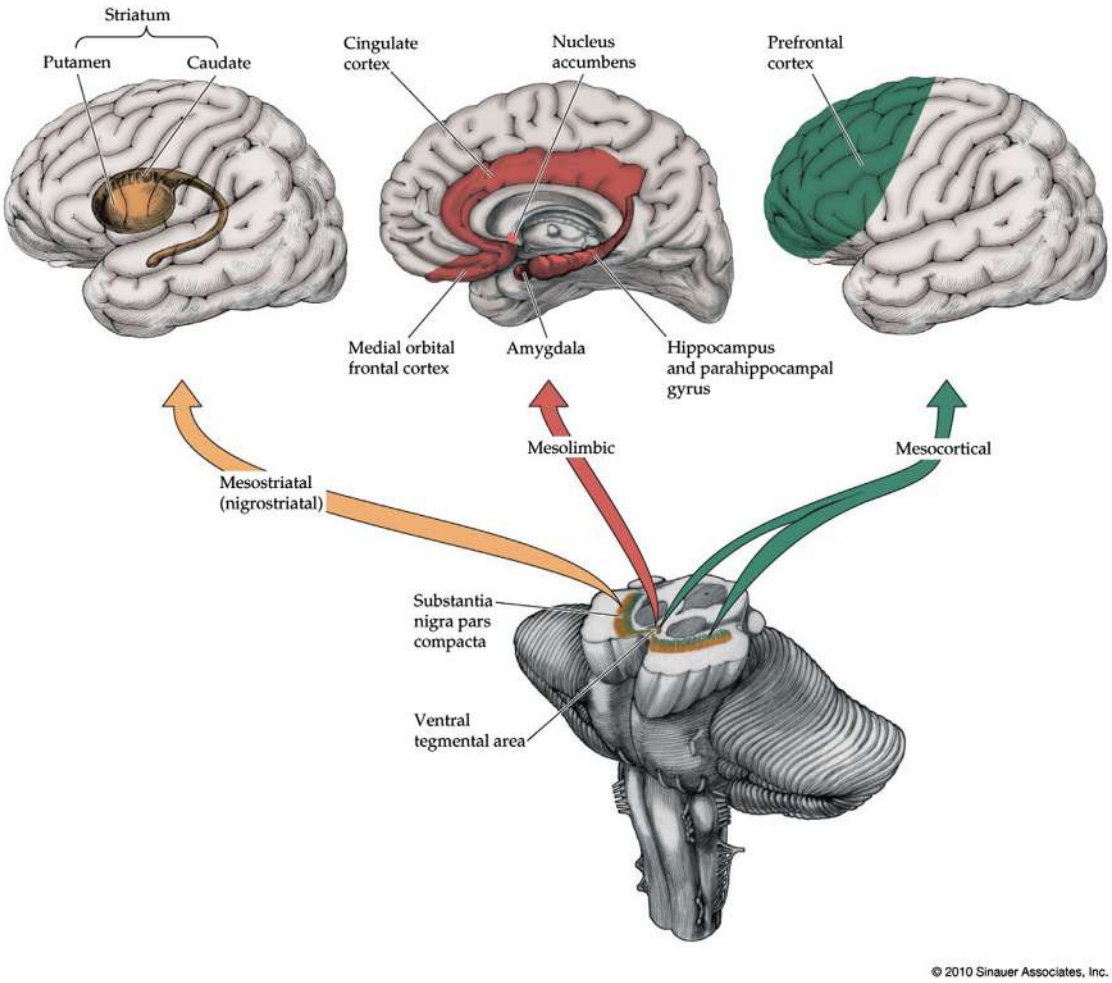

FIGURE 1.9 Dopaminergic projections systems. See also Table 1.1. *Source: Reproduced with permission from Blumenfeld (2010).*

in the ventral tegmental area also project caudally to various brainstem nuclei and to the spinal cord (Oades and Halliday, 1987).

Dopamine may contribute to maintaining the waking state at least in part through effects on other subcortical arousal circuits (Deutch et al., 1986; Lu et al., 2006; Neylan et al., 1992; Qu et al., 2008; Volkow et al., 2009). Effects of dopamine on the thalamus and cortex can be either excitatory or inhibitory (Bandyopadhyay and Hablitz, 2007; Govindaiah et al., 2010; Lavin and Grace, 1998; Penit-Soria et al., 1987). Impaired dopaminergic transmission to the prefrontal cortex has been proposed to be important for the apathetic negative symptoms of schizophrenia, and may also contribute to states of markedly reduced motivation, initiative and action/intention seen in frontal lobe disorders, abulia, and akinetic mutism (Combarros et al., 2000; Kim et al., 2007; Yang et al., 2007). Amantadine improves arousal in chronic disorders of consciousness, although it is unclear whether the mechanism is through enhanced dopaminergic neurotransmission or effects of this medication on other neurotransmitter systems (Giacino et al., 2012).

Histaminergic Arousal Systems

Histamine-containing neurons are found mainly in the tuberomamillary nucleus (Panula et al., 1984) of the posterior hypothalamus (Figure 1.10; Table 1.1), although a few scattered histaminergic neurons are also found in the midbrain reticular formation. Widespread ascending projections of histaminergic neurons from the tuberomamillary nucleus reach nearly the entire forebrain including cortex and thalamus, while descending projections target the brainstem and spinal cord (Brown et al., 2001; Hong and Lee, 2011; Lin et al., 1996; Panula et al., 1989).

Anti-histamine medications are intended to act on peripheral histamine release from mast cells, but are well-known to induce drowsiness presumably through central actions (White and Rumbold, 1988). Histamine can produce arousal effects on cortex (Dringenberg

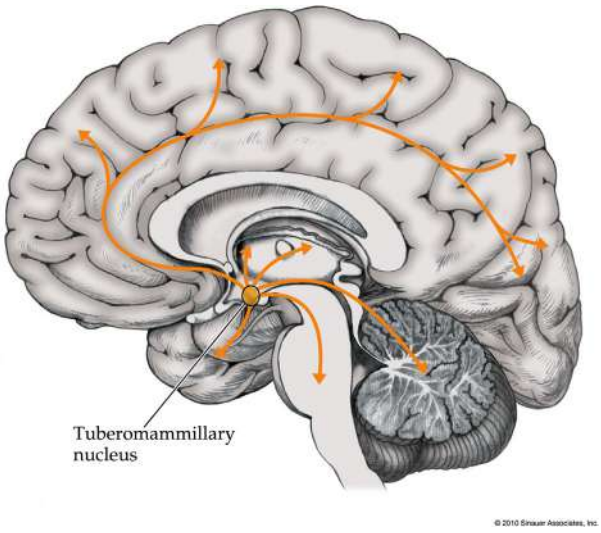

FIGURE 1.10 Histaminergic projections systems. See also Table 1.1. *Source: Reproduced with permission from Blumenfeld (2010).*

and Kuo, 2003; McCormick and Williamson, 1989) and thalamus (McCormick and Williamson, 1991). In addition to the cortex and thalamus, arousal actions of histamine may be mediated by activation of other subcortical arousal systems including other hypothalamic nuclei (Brown et al., 2001; Lin et al., 1994), the basal forebrain (Dringenberg and Kuo, 2003; Khateb et al., 1995; Zant et al., 2012), brainstem cholinergic (Khateb et al., 1990; Lin et al., 1996), and noradrenergic nuclei (Korotkova et al., 2005). Effects of histamine are receptor-dependent as activation of H_1 receptors promotes wakefulness, whereas H_3-receptors appear to have the opposite role (Huang et al., 2006; Khateb et al., 1990; Lin et al., 1990, 1996; Valjakka et al., 1996).

Orexinergic Arousal Systems

Orexin (hypocretin) is a peptide produced in neurons of the perifornical, lateral, and posterior hypothalamus (Peyron et al., 1998; Sakurai et al., 1998), which project to both cortex and virtually all subcortical arousal systems (Chemelli et al., 1999; Peyron et al., 1998) to promote the awake state. The arousal effects of orexin likely arise from both cortical and subcortical mechanisms (Bourgin et al., 2000; Eriksson et al., 2001; España et al., 2001; Hagan et al., 1999; Horvath et al., 1999; Kiyashchenko et al., 2002; Tsunematsu et al., 2011; van den Pol et al., 2002).

Abnormalities of the orexin system are thought to play a role in narcolepsy, a disorder characterized by excessive daytime sleepiness and pathological transitions into rapid eye movement sleep (Anaclet et al., 2009; Chemelli et al., 1999; Gerashchenko et al., 2003; Hara et al., 2001; Lin et al., 1999; Nishino et al., 2000; Peyron et al., 2000; Thannickal et al., 2000). The beneficial effects of modafenil in preventing the symptoms of narcolepsy may in part be through activation of orexin neurons (Chemelli et al., 1999).

Adenosine and Arousal

Although the neuroanatomical sources of adenosine are not well characterized, this neuromodulator may be important in mechanisms of conscious arousal (Huang et al., 2014; Liu and Gao, 2007). The effects of adenosine on arousal are generally inhibitory, and circadian fluctuations in adenosine levels peak just prior to the initiation of sleep. Adenosine receptors are found in both cortex and thalamus, where they have an overall inhibitory function on arousal. Caffeine blocks adenosine receptors and this may be one important mechanism whereby coffee promotes alertness (Huang et al., 2011; Lazarus et al., 2011).

Amygdala and Arousal

Because the amygdala has widespread and reciprocal cortical-subcortical connections that contribute to arousal particularly in response to emotions, it is appropriate to include this complex of nuclei located in the anteromedial temporal lobe as an important subcortical component of the consciousness system (Steriade and McCarley, 2010). The main components of the amygdaloid nuclear complex are the corticomedial, basolateral, and central nuclei, as well as the bed nucleus of the stria terminalis. The basolateral nucleus is largest in humans and has widespread direct and indirect connections to the cortex, basal forebrain, and medial thalamus (Aggleton, 2000; LeDoux, 2007). The smaller corticomedial nucleus participates in appetitive states via the hypothalamus, as well as in olfaction. The central nucleus, although smallest, has important connections with the hypothalamus and brainstem participating in arousal and autonomic control (LeDoux, 2007).

Attention and Awareness: Roles of Subcortical Arousal Systems, Tectal Region, Basal Ganglia, Claustrum, and Cerebellum

To complete our discussion of subcortical networks regulating the level of consciousness, it is important to again emphasize the functions of the consciousness system in controlling alertness, attention, and awareness, and to briefly mention several additional subcortical structures participating in these functions. As we have already discussed, the thalamus and other multiple parallel subcortical arousal systems in the upper brainstem, hypothalamus, and basal forebrain (Table 1.1) are essential for maintaining the alert state.

These same systems also play a key role in controlling attention and awareness not only in a permissive sense (e.g., being in a coma is not compatible with attention and awareness), but also by facilitating the additional processing in cortical and subcortical networks necessary for attention and for awareness.

Several additional subcortical structures also play a role. Components of the tectal region, specifically the superior colliculi and pretectal area form an important circuit along with the pulvinar of the thalamus to direct saccadic eye movements towards salient stimuli, and the same circuits also participate in directed attention (Krauzlis et al., 2013). The basal ganglia have major reciprocal connections with the thalamic intralaminar nuclei and this circuit as well as other basal ganglia connections may contribute to arousal and attention functions (Dreher and Grafman, 2002; Hager et al., 1998; Ring and Serra-Mestres, 2002). The claustrum is a thin layer of neurons located in the white matter between the putamen and insula, with widespread cortical connections that have been proposed to play an important role in the attention and awareness aspects of consciousness (Crick and Koch, 2005). Finally, the cerebellum has major reciprocal connections with the prefrontal cortex and has also been proposed to participate in attention, although this remains somewhat controversial (Baumann and Mattingley, 2014; Bischoff-Grethe et al., 2002; Dreher and Grafman, 2002; O'Halloran et al., 2012).

CORTICAL NETWORKS AND CONSCIOUSNESS

The cortical components of the consciousness system include widespread regions of association cortex in the bilateral cerebral hemispheres, particularly in the lateral frontal, anterior insula, lateral parietal (and adjacent temporal-occipital cortex), medial frontal, medial parietal (precuneus) and cingulate cortex (Figure 1.2). As has already been discussed, individual cortical components of the consciousness system have specific well-studied functions in behavioral neurology which contribute to the various contents of consciousness along with specific primary and secondary sensorimotor and limbic cortical areas (Figure 1.11). However, it is the collective action of widespread bilateral association cortex regions that gives rise to regulation of the level of alertness, attention, and conscious awareness.

In this section we will review the contributions of the cerebral cortex to arousal and the generation of an alert, awake state. We will next discuss attention in somewhat greater detail, describing several formulations of cortical systems that control different aspects of attention. The relationship between memory systems and consciousness will then be considered, as well as the role of cortical networks in self-awareness, planning voluntary action and free will. Finally, we will review cortical networks revealed by contrastive analysis (perceived vs non-perceived stimuli) to play an important role in conscious awareness.

The Cortex and Arousal

The most important input to subcortical arousal systems, including the thalamus, hypothalamus, basal forebrain, and the multiple brainstem arousal systems is the cerebral cortex itself. It has long been known that stimulation of the higher-order heteromodal frontoparietal association cortex increases arousal (Figure 1.11) (Segundo et al., 1955). Conversely, ablation of these same regions of the higher-order association cortex markedly decreases arousal (Ropert and Steriade, 1981; Steriade and McCarley, 2010; Watson, et al., 1977), although the subcortical arousal systems also receive inputs from primary sensorimotor cortices (Catsman-Berrevoets and Kuypers, 1981; Ropert and Steriade, 1981; Rossi and Brodal, 1956). In further support of the importance of the cerebral cortex in maintaining consciousness it was recognized by clinicians that unilateral cortical lesions usually do not markedly depress level of consciousness, but bilateral lesions of the association cortex can produce coma (Plum and Posner, 1972; Posner et al., 2007). The parietal cortex of the non-dominant (usually right) hemisphere appears to play a particularly important role in arousal where large lesions—although not producing coma—do often produce a markedly drowsy clinical state with forced eye closure. Thus, in addition to its important role in producing the specific individual contents of consciousness, the cerebral cortex is also a major driver in regulating the overall level of conscious arousal.

Attention and Consciousness

There has been recent debate on the relationship between attention and consciousness. Some view attention and consciousness as orthogonal functions that can be fully dissociated and operate independently (Koch and Tsuchiya, 2007). Others consider attention and consciousness to be essentially identical, constituting different names for the same set of functions (Prinz, 2000, 2012). Still others posit that attention is necessary for but not identical to consciousness because additional functions are needed for conscious awareness (Dehaene et al., 2006; Kouider and Dehaene, 2007). These very different understandings of the relationship between attention and consciousness may arise at least in part from different models for defining and understanding attention. There are a large number

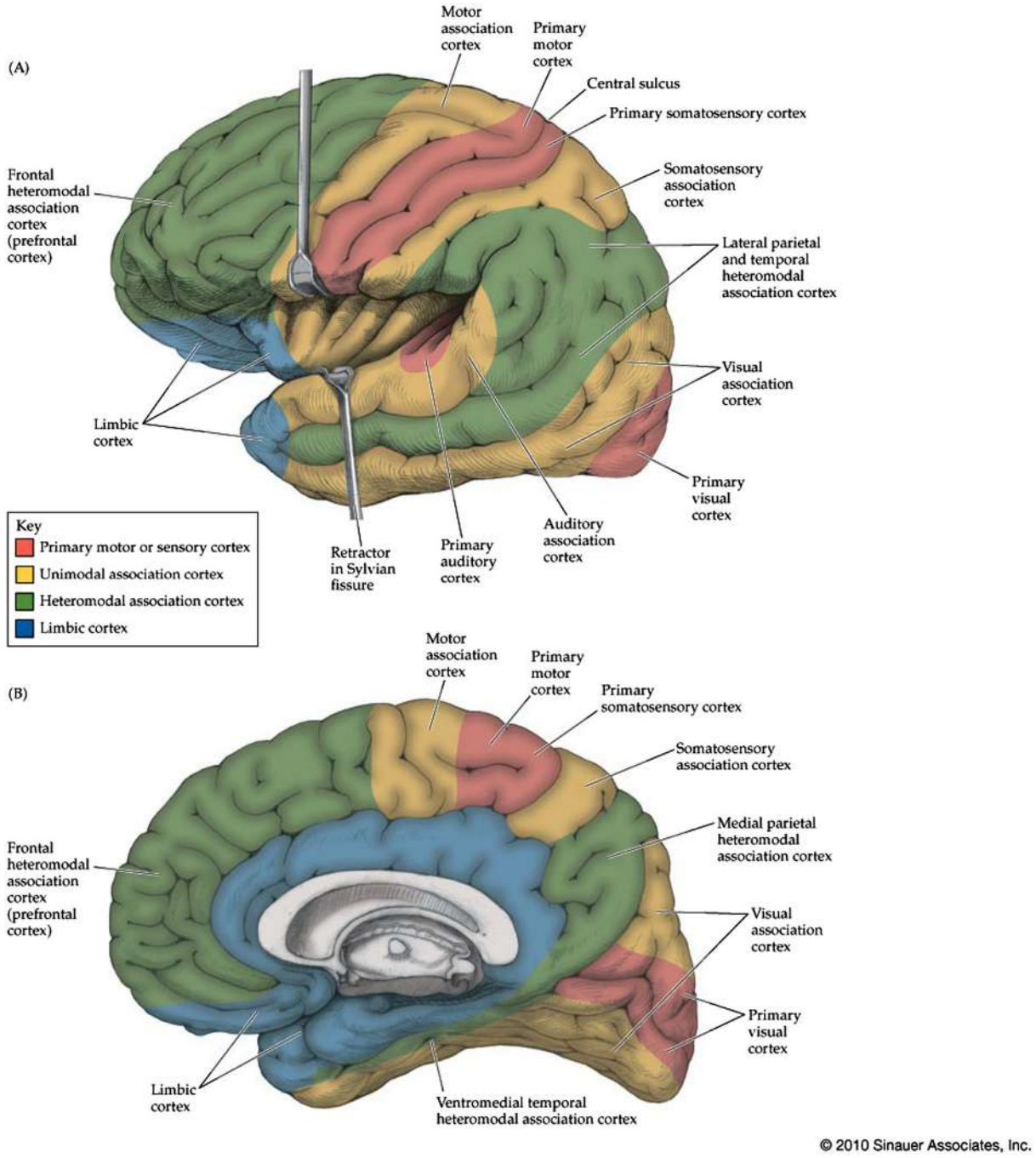

FIGURE 1.11 Cerebral cortex. (A) Lateral view. (B) Medial view. Main primary cortical and association cortical areas are indicated. Unimodal association cortex is modality-specific, whereas higher-order heteromodal association cortex combines information across modalities. Regions labeled here as limbic cortex include allocortical regions such as the hippocampus (archicortex) and pyriform cortex (paleocortex) as well as transitional paralimbic and neocortical areas such as the parahippocampal gyrus, cingulate gyrus, anterior insula, orbitofrontal cortex, and temporal pole. *Source: Reproduced with permission from Blumenfeld (2010).*

of models of attention and a complete discussion of the anatomy of attention is far beyond the scope of this chapter. However, here we will at least discuss a few of the major current formulations of attention especially in how their cortical anatomical underpinnings relate to understanding consciousness.

Hemispheric Dominance of Attention

Even more than the laterality of language, spatial attention is strongly lateralized and the large majority of individuals have dominant spatial attention in the right hemisphere (Heilman and Valenstein, 2003; Heilman et al., 2000; Mesulam, 2000). Contralateral

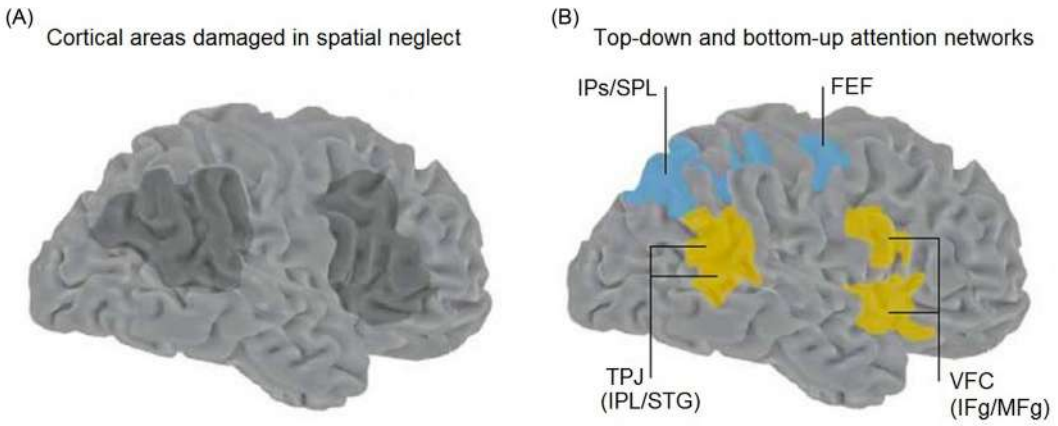

FIGURE 1.12 Top-down, bottom-up attention networks and hemineglect. (A) Areas commonly damaged in the right hemisphere that cause the contralateral hemineglect syndrome. (B) Dorsal and ventral frontoparietal attention. Areas in blue indicate the dorsal frontoparietal "top-down" attention network. FEF, frontal eye field; IPs/SPL, intraparietal sulcus/superior parietal lobule. Areas in orange indicate the stimulus-driven ventral frontoparietal "bottom-up" attention network. TPJ, temporoparietal junction (IPL/STG, inferior parietal lobule/superior temporal gyrus); VFC, ventral frontal cortex (IFg/MFg, inferior frontal gyrus/middle frontal gyrus). The areas damaged in neglect (A) better match the ventral network. *Source: Modified with permission from Corbetta and Shulman (2002).*

attentional neglect is more common and usually far more severe with lesions of the right hemisphere, especially with damage to the right lateral parietal cortex, although hemineglect can also be seen with right frontal lesions (Figure 1.12A). Unilateral neglect profoundly impairs the affected individual's ability to attend to visual, auditory, and tactile stimuli, to motor intention and indeed even to the very existence of the entire contralateral half of their body and the external world opposite to the side of their lesion. Although the impaired attention is usually most profound contralateral to right hemisphere lesions, there is also some attentional impairment which extends to the ipsilateral side so that overall attention is globally decreased (Heilman et al., 2000). Milder degrees of unilateral contralateral neglect are usually seen with left lateral parietal or left frontal lesions. Overall, these features of the neglect syndrome support a model in which attention functions are distributed between the association cortices in both hemispheres, but with a dominant role played by the right lateral parietal and frontal association cortex.

Some, even as early as Descartes, have argued that language is necessary for conscious thought (Descartes, 1637/1988, 1649/1970) and because the left hemisphere is usually dominant for language it could be viewed as more important for consciousness than the right. However, clearly non-verbal thoughts can still generate conscious experiences (Devinsky, 2000). Therefore, language might best be viewed as an important component of the content of consciousness (along with other specific functions such as visual perception, mathematical ability, judgment of distance, and so on), rather than as a necessary regulator of the overall level of consciousness. In some studies impaired consciousness is more common when the left hemisphere is impaired for example, due to stroke, or during selective administration of barbiturate anesthetics to one hemisphere at a time in the angiogram Wada test (Albert et al., 1976; Franczek et al., 1997; Schwartz, 1967), or with focal seizures originating in the left hemisphere (Englot et al., 2010; Gabr et al., 1989; Inoue and Mihara, 1998; Lux et al., 2002). However, it is difficult to determine whether a bias of testing methods which are heavily weighted towards verbal rather than non-verbal questions and responses might strongly influence these finding.

Affect, Motivation, and Attention

One important aspect of cortical attention networks that should not be overlooked is the major role of affect and motivational drives (Damasio and Carvalho, 2013; Heilman and Valenstein, 2003; Heilman et al., 2000; Satz and Heilman, 1983). Subjects who are emotionally motivated, for example, by seeking a reward, are clearly more successful in attention tasks (Heilman and Valenstein, 2003). The orbital frontal cortex and other limbic circuits have been implicated and are likely to be crucial for the motivational aspects of attention (Faw, 2003).

The Binding Problem

A classical quandary in understanding attention and consciousness is the question of where and how the diverse aspects of any particular percept come together to form a unified conscious experience. How do the look, smell, and sound of your friend come together in your brain as "Adam." Even within a

single modality, it is challenging to understand how for example, the different parts of a visual scene are unified as whole image. This question has been referred to as the binding problem (Singer, 2001). Many potential solutions have been proposed for how different components of sensory input are bound together into a single percept, including coherent high-frequency oscillations, lateral connections between neurons in particular cortical layers, among others (Singer, 2001; Zmigrod and Hommel, 2013). In terms of cortical anatomy some insights into how visual binding occurs may be gleaned from a particular disorder referred to as Balint syndrome (Barton, 2011; Heilman and Valenstein, 2003; Michel and Henaff, 2004). Patients with Balint syndrome experience simultagnosia, meaning that they perceive individual fragments or components of a visual scene one at a time without assembling them into a coherent whole. Balint syndrome is caused by bilateral lesions at the juncture between the dorsolateral parietal and occipital cortices (often due to strokes in the watershed territory between the posterior and middle cerebral arteries). It has been proposed that simultagnosia occurs because these lesions disconnect visual input from parietal and other association cortices needed to stitch together the individual components into a unified image. This suggests that one mechanism for attentional binding may be the interaction of primary cortices or unimodal association cortex with higher-order (heteromodal) parietal or other association cortices (Figure 1.11). In this case, one would predict that simultagnosia should occur not just in visual but in other (e.g., auditory or tactile) modalities when unimodal cortices are disconnected from the higher-order association cortex bilaterally, a topic for potential additional investigation in future work.

Top-Down and Bottom-Up Attention Networks

Emerging from other recent formulations of attention, including those proposed by Mesulam, Heilman, and Posner (Heilman and Valenstein, 2003; Mesulam, 2000; Posner and Dehaene, 1994; Posner and Petersen, 1990), the model of Corbetta and Shulman (2002) emphasizes two separate but interacting systems mediating the top-down and bottom-up aspects of attention (Figure 1.12B). In this scheme, goal-oriented selection of stimuli and responses is controlled by dorsal regions of the frontal and parietal association cortex, including the frontal eye fields and intraparietal sulcus. This top-down attention system is bilaterally distributed in both hemispheres. In contrast, a second attention system serves a stimulus-driven "circuit-breaking" role for grabbing and reorienting attention in response to salient or changing sensory stimuli. This bottom-up attention system is localized more ventrally in the temporal-parietal junction and the ventral frontal cortex (including the frontal operculum), and is strongly lateralized to the right hemisphere. One important area of ongoing research is how the two systems interact, for example, during stimulus-driven reorienting in visual search where sensory inputs affect goal-oriented attention and vice-versa.

Task-Positive and Task-Negative Networks

Another important way of describing cortical attention networks has arisen from functional neuroimaging studies during tasks compared to rest, as well as the analysis of resting functional connectivity. In a series of observations by Raichle et al. (2001), Shulman et al. (1997) and subsequently confirmed by other groups it was noted that, regardless of the specific task, a particular set of regions tends to show reduced activity during task blocks when functional neuroimaging data are analyzed by conventional block-design analyses contrasting task versus rest. These brain regions were dubbed the "default-mode network" (hypothesized to be relatively active at rest by default) or "task-negative networks." On the other hand, regions showing relatively increased activity during task blocks show greater variability depending on the specific task, but do show some general similarities between studies—particularly those involving attention—and have been referred to as "task-positive networks." Of interest, like many other important brain networks (Biswal et al., 1995, 1997), the default-mode and task-positive networks can be demonstrated in functional neuroimaging studies based on their high within-network connectivity using resting data in the absence of task (Fox et al., 2005; Fransson, 2005; Greicius et al., 2003). At rest, the default-mode and task-positive networks demonstrate high within-network functional connectivity (correlations over time) and these two networks are overall negatively correlated with each other (Figure 1.13). Based on both task-related analyses, and resting connectivity analyses, the default-mode network generally includes the following cortical regions bilaterally: precuneus/posterior cingulate, posterior-inferior parietal lobule (angular gyrus), ventral-anterior medial frontal, middle temporal gyrus, and medial temporal cortex (Figure 1.13) (Fox et al., 2005). The task-positive networks include the following cortical regions bilaterally: anterior insula/frontal operculum, supplementary motor/dorsal medial frontal lobe, lateral premotor cortex (includes frontal eye fields), anterior middle frontal gyrus, superior parietal lobule/anterior inferior parietal lobule, lateral inferior posterior temporal gyrus (lateral area 37) (Figure 1.13).

Because the concept of two large anti-correlated networks mediating attention switching in the brain may be over-simplified, a number of groups have

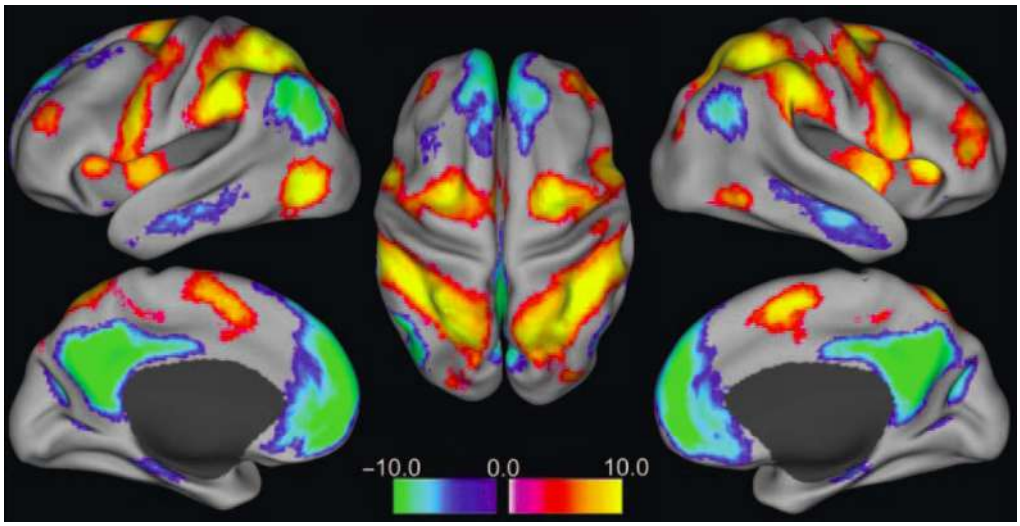

FIGURE 1.13 Task-positive and default-mode (task-negative) networks by resting functional connectivity analysis. A conjunction analysis was performed by including voxels significantly positively or negatively correlated with three seed regions in the task-positive network (intraparietal sulcus; frontal eye fields; lateral posterior-inferior temporal region) and three in the default-mode network (ventral medial prefrontal cortex; posterior cingulate/precuneus; lateral parietal cortex). Warm colors show regions correlated with the task-positive seeds or negatively correlated with default-mode seeds. Cool colors show regions correlated with the default-mode seeds or negatively correlated with task-positive seeds. *Source: Reproduced with permission from Fox et al. (2005).*

attempted to further refine these ideas and the field is still very much in evolution. It has been proposed that certain components of the task-positive network, referred to as the frontal parietal control network, might play a role in switching between externally directed attention mediated by the dorsal attention network (similar to top-down attention areas of Corbetta and Shulman discussed above) and internally directed attention mediated by the default-mode network (Gao and Lin, 2012; Vincent et al., 2008). There is evidence that the more lateral components of the task-positive network, particularly the dorsolateral frontal and parietal cortices are more important for externally directed attention, while the medial components of the default-mode network participate in internally directed attention (Demertzi et al., 2013; Vanhaudenhuyse et al., 2011). In another series of studies, Dosenbach et al. (2006, 2007, 2008) identified certain bilateral core components of the task-positive network, namely the dorsal anterior cingulate/medial superior frontal cortex (and adjacent supplementary motor area), and anterior insula/frontal operculum which constitute a common network involved in: (i) task initiation, (ii) sustained activity, and (iii) error detection (Figure 1.14). In contrast, they found that other areas in the task-positive and default-mode networks are activated or inactivated less consistently in these three different conditions. Again it is unclear if the functional imaging signals in anterior insula, which play a prominent role in this network, could also have a contribution from the nearby claustrum, a subcortical structure discussed above that might participate in attention and consciousness. In additional analyses based on resting functional connectivity and graph theory, the same group again emphasized the importance of what they refer to as the cingulo-opercular network, as distinct from the other task-positive and default-mode network nodes (Dosenbach et al., 2007). Another very interesting approach has been model-free analysis of functional neuroimaging data by simply using massive averaging of large data sets during a simple attention task (Gonzalez-Castillo et al., 2012). This type of analysis revealed that virtually the entire brain shows signals that vary over time in relation to the task, with a combination of transient or sustained increases and/or decreases depending on the specific brain region.

In summary, a large number of cortical networks have been shown to participate in different aspects of attention and to modulate their activity in relation to onset and end of attention tasks. The detailed roles that different components play in attention and consciousness, including anterior insula/frontal operculum, dorsal attention, default-mode, task-positive, bottom-up, top-down and other networks, will be important subjects for further investigation.

Memory Systems and Consciousness

As we have discussed, the level of consciousness depends on regulation of alertness, attention, and awareness. Alertness (arousal, wakefulness) can be

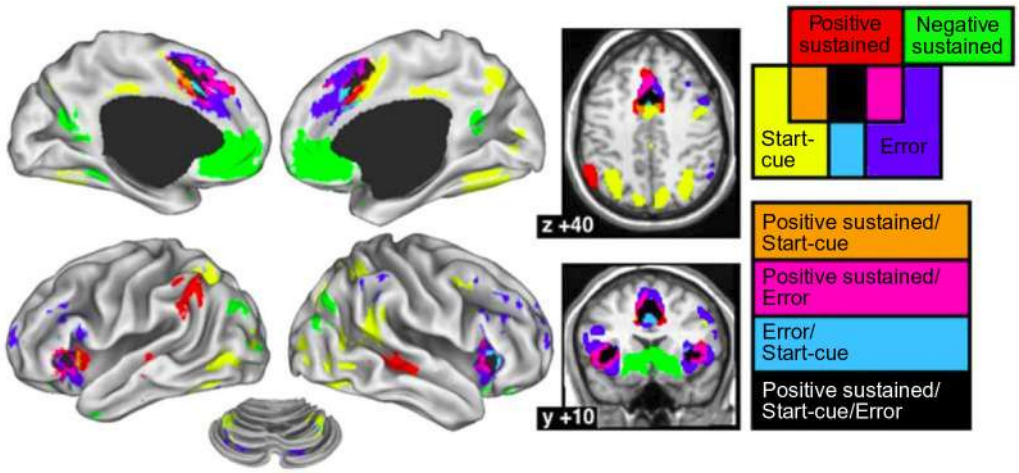

FIGURE 1.14 Core components of human task-related networks. Conjunction analysis of the fixed-effects maps for positive sustained, start-cue and error-related activity. The dorsal anterior cingulate/medial superior frontal cortex (and adjacent supplementary motor area), and anterior insula/frontal operculum carried positive sustained, start-cue and error-related activity across most of the tasks included in the analysis (conjunction regions shown in black). *Source: Reproduced with permission from Dosenbach et al. (2006).*

tested based on responses to simple questions or commands, and attention based on tasks requiring selective responses. Awareness, on the other hand, is demonstrated when a subject reports being aware of a particular stimulus or event. Because this report inevitably occurs after the event, testing of conscious awareness requires memory. Memory therefore plays a crucial role in the ability to report conscious experiences. In fact it may be useful to define awareness as the attentive and other processes necessary for events to be selected, handed off and encoded into memory for subsequent report.

Depending on whether report of conscious awareness occurs following a short or long delay, different memory systems may participate. Immediate recall or iconic memory most likely involves activity in primary and unimodal cortices and where events are initially processed (Coltheart, 1980; Loftus et al., 1992). Slightly more enduring memories lasting several seconds can enter working memory systems involving the dorsolateral frontal and parietal association cortices (Funahashi et al., 1993; Ikkai and Curtis, 2011). Some have defined consciousness based on the transfer of attended events into working memory (Prinz, 2012). Long-term memory storage of facts and autobiographical events requires the action of medial temporal and medial diencephalic memory circuits (Squire and Wixted, 2011; Tulving, 2002). Episodic or declarative memory, which depends on these anatomical systems, can be considered conscious memory in contrast to unconscious procedural memory that involves learning skills or unconscious priming. Because medial temporal and medial diencephalic memory systems are so specifically linked to the encoding of conscious experiences for subsequent report, investigating the "gateway" leading into these systems may be a productive approach for understanding the mechanisms of conscious awareness.

Volition and Conscious Free Will

Although much research has been done in the field of conscious perception particularly emphasizing the visual system, an equally important area of investigation is the mechanisms of conscious action including those governing planning and initiation of voluntary movement (Roskies, 2010). Understanding conscious action has important implications for determining moral and legal responsibility, as well as philosophical relevance including the definition of free will. Conscious action can be divided into planning, "premeditation" or initiation of future activities, and awareness of ongoing or completed deeds. The latter is more similar to conscious sensory perception, in the sense that it involves subsequent report of events that have already taken place. Conscious planning and initiation of voluntary movement as well as decision making on the other hand, likely involve other neuroanatomical circuits, as we will briefly discuss further below.

Motor planning depends on a distributed network including the premotor, supplementary motor and other frontal cortical circuits, interacting with parietal association cortex and subcortical networks especially in the basal ganglia (Roskies, 2010). Decision making is likewise a growing field in neuroscience, and recent work has again implicated distributed frontoparietal and subcortical circuits (Glimcher, 2003; Lau and Glimcher, 2008; Levy et al., 2010; Platt and Glimcher,

1999; Roskies, 2010). Based on stimulation mapping, some interesting dissociations have been found. Stimulation of the parietal cortex is accompanied by an awareness of voluntary movement initiation or urge to move even if no actual motion takes place (Desmurget et al., 1999, 2009; Desmurget and Sirigu, 2009). On the other hand, stimulation of the premotor cortex of the frontal lobe can produce actual movement even when the subject is unaware of the movement (Desmurget et al., 2009; Roskies, 2010). Finally, stimulation of the supplementary motor area produces an urge to move that may feel compulsory or involuntary (Fried et al., 1991).

Spontaneous voluntary movements are preceded 1−2 s earlier by a "readiness potential" or "Bereitschafts potential" that can be recorded from the scalp near the midline and has subsequently been localized to the supplementary motor area based on intracranial measurements (Fried et al., 2011). In a thought-provoking study, Benjamin Libet famously examined the timing of the readiness potential and provided evidence that it may precede the moment when individuals become consciously aware of their decision or will to move by several hundred milliseconds (Libet et al., 1982, 1983a,b). The interpretation of this study and its relation to free will has been hotly debated in later work (Herrmann et al., 2008; Jo et al., 2013; Schurger et al., 2012).

Self-Awareness and Embodiment

Although some consider self-awareness to be the defining *sine qua non* of consciousness, others view awareness of self to be just one example of the many things that an individual can be aware of, and therefore not necessary or sufficient for consciousness (Zeman, 2005). A closely related topic is the ability to have a first-person perspective or sense of embodiment arising from one's own individual point of view, which clearly makes an important contribution to the subjective feeling of awareness.

Awareness of self can be drastically and selectively impaired in certain neurological disorders, which may provide some insight into the neuroanatomical basis of self-awareness. For example, patients with lesions in the non-dominant (usually right) hemisphere particularly in the lateral parietal cortex are often agnostic to the very existence of the entire left side of their own bodies, and when specifically asked sometimes consider their left limbs to belong to someone else (Heilman et al., 2000). Frontal lobe dysfunction commonly leads to impaired self-monitoring or self-awareness, and is thought to underlie patient's inability to recognize their own deficits, for example when some patients confabulate instead of admitting to amnesia (Kopelman, 2014). One specialized form of self-awareness is awareness of one's own conscious awareness. This form of meta-cognition is also an important topic of investigation that may shed insights into what many consider the highest forms of consciousness (Zeman and Coebergh, 2013).

Important advances have recently been made in understanding the mechanisms that provide a first-person perspective by the innovative studies of Olaf Blanke and colleagues (Blanke, 2004; Blanke et al., 2002; Easton et al., 2009; Heydrich et al., 2010; Lenggenhager et al., 2009; Lopez et al., 2010). A series of investigations using patients with out-of-body experience, or functional neuroimaging and behavioral interventions to create an out-of-body experience in normal subjects, have revealed that the right temporal-parietal junction plays a crucial role in this unusual condition. Additional insights may come from ongoing investigation of other situations where the first-person perspective is altered, for example, during early development or in psychiatric disorders where depersonalization can occur (Bunning and Blanke, 2005; Lewis, 2011; Sierra and David, 2011).

Awareness: Conscious Report and Contrastive Analysis

Philosophers and scientists have long enjoyed a debate about whether or not consciousness can be understood through scientific investigation. The crux of the argument rests on the definitions of "consciousness" and "understanding." Some define the qualitative phenomenal aspects of consciousness or qualia, as internal subjective feelings of awareness accessible only through first-person experience, and define understanding consciousness as having that first-person experience (Chalmers, 1996). These definitions automatically exclude the possibility of understanding consciousness through scientific means because science requires external second-person observations. On the other hand, if one defines conscious awareness as an experience that can be described or reported to others, and if one defines understanding consciousness as identifying the necessary and sufficient physiological mechanisms for such an experience, then consciousness falls clearly in the realm of scientific investigation. The key to this second approach is that external report of consciousness is allowed as a method for investigating consciousness. Report of consciousness has its limitations of course, but so do all scientific methods and as long as the limitations are recognized and results interpreted cautiously, much progress can be made.

Taking this approach, a large number of studies have investigated the contrast between brain activity when a conscious event is reported or is not reported under very similar circumstances. This contrastive analysis has been performed in a variety of situations where events that are or are not reported can be obtained (Dehaene and Changeux, 2011; Lamme, 2006; Tononi

and Koch, 2008). For example, presentation of visual, tactile, or other stimuli at the threshold of detection yields approximately 50% that are reported. These studies have shown that consciously reported stimuli are accompanied by significantly greater activity in the bilateral frontal and parietal association cortex than with the unreported stimuli (Li et al., 2014; Palva et al., 2005; Wyart and Tallon-Baudry, 2008). Similarly, post-hoc analysis of items presented during memory encoding has demonstrated increased activity in fronto-parietal cortex during presentations of items that are later successfully reported (Burke et al., 2014). Another paradigm has been binocular rivalry, in which one image is presented to the left eye and a different image to the right eye, causing the perceived image to randomly alternate every few seconds between the two images (Blake and Logothetis, 2002; Polonsky et al., 2000). It was found that these alternating experiences can be related to alternating activity between different neurons in the temporal and parietal association cortex, particularly in a visual association cortex region in the inferior temporal lobe. Other paradigms including masking of visual stimuli by flanking stimuli presented immediately before or after the target, or use of the "attentional blink" have also been employed to control whether or not stimuli are perceived and consciously reported, again showing that consciously perceived stimuli have greater activations including larger neuroimaging signals, event-related potentials, or synchronized oscillations in the frontal and parietal association cortex (Dehaene and Changeux, 2011; Del Cul et al., 2009; Kouider and Dehaene, 2007; Marois et al., 2004).

In summary, multiple studies using contrastive analysis have demonstrated that events reported as consciously perceived give rise to greater activity in the bilateral frontal and parietal association cortex. These findings support the idea that the anatomical regions constituting the consciousness system (Figure 1.2) play an important role in regulating conscious awareness. Further work is needed to more firmly establish that these areas are necessary and sufficient for conscious events, for example through lesion/inactivation and activation studies. In addition, although much has been learned about the neuroanatomical structures participating in consciousness, further investigation will be crucial to firmly establish the physiological mechanisms through which consciousness is generated in these networks.

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